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The Effects of Insoluble Fiber Supplementation
In An Outpatient Hemodialysis Population

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Marci Lee Askegard

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THE EFFECTS OF INSOLUBLE FIBER SUPPLEMENTATION IN AN OUTPATIENT HEMODIALYSIS POPULATION

By

Marci Lee Askegard

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ABSTRACT

THE EFFECTS OF INSOLUBLE FIBER SUPPLEMENTATION IN AN OUTPATIENT HEMODIALYSIS POPULATION

By

Marci Lee Askegard

The effects of insoluble fiber (14g from pea, oat, and sugar beet) supplementation on laxation, food intake, serum constituents and diet/medication compliance were determined in 15 adult hemodialysis outpatients using a 57-day cross-over design. Fiber supplementation did not produce adverse gastrointestinal effects, change diet/medication compliance, or decrease food intake. There were no significant differences in body weight (dry), interdialytic weight gain, stool number/consistency or serum BUN, creatinine, phosphorus, glucose, iron, cholesterol, HDL-cholesterol, triglycerides, or ferritin. Decreased serum potassium and calcium occurred with treatment. Fiber supplementation normalized bowel function in over half the subjects although constipation was not a criterion for study participation. Insoluble fiber supplementation from pea, oat and sugar beet for three weeks produced no serious side effects and may be useful short-term therapy in dialysis patients. Further investigation of long-term effect on serum calcium should be conducted before recommending long-term use.

DEDICATION

In honor of my parents Ronald D. and Cecelia A. Askegard,
and grandparents: Gerald F. and Mary Watson,
Mildred V. Askegard, and the late Harry Louis Askegard
who instilled in me a trust in the Lord and my own abilities,
and the desire to set goals that test and maximize those abilities.

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CHAPTER I

INTRODUCTION

Statement of the Problem

End stage renal disease patients on hemodialysis have unique dietary and fluid restrictions as part of their daily medical therapy. These restrictions, as well as medications, lack of exercise, and other factors can result in constipation as a complication in many hemodialysis patients. These patients also may suffer from additional complications such as diabetes and hyperlipidemias.

Fiber supplementation would be a possible valuable addition to the current nutritional regimen used with hemodialysis patients, if the benefits of fiber supplementation can be shown to outweigh possible problems or side effects. Studies to determine the benefits and disadvantages of adding fiber to the diet of renal patients were very sparse in the literature reviewed.

Purpose of the Study

The purpose of this investigation was to study the effects of insoluble fiber supplementation in End Stage Renal Disease (ESRD) patients residing in central Michigan who have hemodialysis treatments at Sparrow Hospital. Fiber in relation to laxation, food intake, selected blood constituents (serum potassium, phosphorus, calcium, cholesterol, triglycerides, lipoproteins, urea, creatinine, glucose, iron, and ferritin), diet/medication compliance, and acceptability of the fiber supplement product were measured.

The independent variable was the fiber supplement (or no fiber supplement). The dependent variables were acceptability of the fiber supplement product; laxation; consistency and number of stools; selected gastrointestinal disturbances (cramping, constipation, diarrhea, rumbling, gas, nausea); adherence to diet, and actual food intake as measured by diet record analysis; adherence to medication regimens as measured by medication records; serum values of potassium, phosphorus, calcium, cholesterol, triglyceride, lipoproteins, urea, glucose, and ferritin; and weight stability in relation to interdialytic weight gains. The investigation was designed to analyze the effects of the independent variable on the dependent variables when the subjects were placed on each treatment for three weeks in a cross-over design.

Hypotheses

There were several main hypotheses, as well as two secondary hypotheses which were to be tested by this study.

Main Hypotheses:

1. Fiber supplementation will be effective in treating /preventing constipation in the renal hemodialysis patient.
2. Fiber supplementation will not increase adverse gastrointestinal symptoms (cramping, bloating, gas, diarrhea, etc,) in the renal hemodialysis patient.
3. Fiber supplementation will not reduce food intake of the renal hemodialysis patient.
4. Fiber supplementation will not affect the fasting blood concentrations of potassium, phosphorus, calcium, cholesterol, triglycerides, lipoproteins, urea, glucose, creatinine, iron, or ferritin in the renal hemodialysis patient.
5. Fiber supplementation, in the form of a fiber cookie, will be an acceptable (palatable) way to incorporate fiber into the diet of the renal hemodialysis patient.

Secondary Hypotheses:

1. Fiber supplementation will not affect the dry weights or between dialysis weight (interdialytic) gains in the renal hemodialysis patient.
2. Fiber supplementation will not affect the diet or medication compliance of the renal hemodialysis patient.

CHAPTER II

REVIEW OF THE LITERATURE

Introduction

Presently, more than 90,000 patients worldwide (>85,000 in the United States) are suffering from chronic renal failure (End Stage Renal Disease), and rely on treatment with either dialysis or transplantation for survival. This number continues to increase each year (Amend et al., 1988). The typical hemodialysis patient has lost >90 % of normal glomerular function due to illness or disease. Hemodialysis replaces the filtering functions of the diseased kidney. The hemodialysis patient spends an average of 10-15 hours a week on a dialyzing machine which filters from the blood the excess water and low molecular weight substances (such as potassium, phosphates, sulfates, urea, creatinine, and uric acid) that are harmful or toxic to the body (Zeman, 1983, 1990).

For some patients with chronic renal failure, hemodialysis, in combination with a diet controlled in protein, sodium, potassium, phosphorus, and/or fluid, may be used for an extended period of time (i.e. >20 years) as therapy (Anon, 1984; Burton et al., 1983; El Nahas, 1986; Mitch et al., 1981; Zeman, 1983). With such dietary restrictions, the consumption of fruits, vegetables, and whole grains is limited due to their content of one or more of the previously stated nutrients.

With the limitation of these foods in the diet, the fiber content of the diet also may be low.

Types of Dietary Fibers

Review of the literature produces evidence that there is not a precise or universally accepted definition of dietary fiber (AMA Council on Scientific Affairs, 1989). Dietary fiber has been defined as "all nondigestable cell wall components, including cutins, waxes, and other coat materials" (Anderson, 1986). Fleming et al. (1986) developed a working definition of fiber as: "the plant polysaccharides and lignin which are resistant to hydrolysis by the digestive enzymes of man." Dietary fiber can be classified into noncellulosic polysaccharides (including hemicelluloses, pectic substances, mucilages, gums, and algal polysaccharides), cellulose, and lignin (Simpoulos, 1986; Slavin, 1987) and is found only in plant products such as fruits, vegetables, nuts, and grains.

Dietary fiber can also be classified into two broad categories based on water solubility, water soluble and water insoluble. The water-insoluble fibers are measured by the neutral detergent residue method of Goering and Van Soest (Goering et al., 1970) and include the celluloses, lignins, and many hemicelluloses. Major food sources of water insoluble fibers are wheat, grains, and vegetables. Insoluble fibers have water holding capacity and a tendency to reduce or relieve constipation when fluid intake is adequate (AMA Council on Scientific Affairs, 1989; Anderson, 1985; Yen, 1988). The water soluble fibers are estimated by the technique of Southgate (1969) and include the pectins,

gums, certain hemicelluloses, mucilages, and storage polysaccharides. Major food sources of the water soluble fibers include fruits, legumes, oats, and barley (Anderson, 1987; Fleming et al., 1986). Diets with certain types of soluble fibers have been shown to lower blood cholesterol levels in specific patient populations that exhibit elevated serum cholesterol and to lower blood glucose levels in patients with diabetes (Anderson, 1980; 1985; 1987; Fleming et al., 1986; Hagander et al., 1989). Whether the lowering of serum cholesterol is due to a direct effect of the soluble fiber or to decreasing fat content of the diet is still under investigation.

Plant gums (such as xanthan gum) are a complex group of highly branched polysaccharides containing glucuronic and galacturonic acid as well as xylose, arabinose, and mannose (Anderson, 1979).

Dietary Fiber and Health

Based on epidemiological data of low incidence of Western diseases (such as colon cancer, coronary heart disease, obesity, diabetes, and hypertension) in an African population which consumed traditional unrefined diets, Burkett and Trowell (in the 1970's) hypothesized a link between the Westernized low fiber intake and an increase in those diseases. Although this link did not demonstrate cause and effect, current clinical research does support the hypothesis in relation to certain diseases including glucose homeostasis in diabetes, certain types of hyperlipidemias, constipation, and several gastrointestinal disorders (Anderson, 1990; 1986; Astrup, 1989; Trowell et al., 1985).

Cummings (1978), in a review of the literature concerning the nutritional implications of dietary fiber, concluded that dietary fiber appears to affect the rate and route of absorption and metabolism of dietary fat, carbohydrate, and protein. Dietary fiber may also alter sterol metabolism, as well as vitamin and mineral absorption and metabolism.

A diet that includes foods high in fiber such as fruits, vegetables, and whole grains is recommended by professional organizations (including The National Institutes of Health, The American Cancer Society, The National Academy of Sciences, and The American Dietetic Association), as a way to promote health, while decreasing the risk for certain diseases (American Cancer Society, 1984; ADA Reports, 1988; National Academy of Sciences, 1982; National Cancer Institute, 1984) . Although no Recommended Dietary Allowance exists for dietary fiber intake, a report prepared for the US Food and Drug Administration does recommend a daily dietary fiber intake of 20-35 grams (Anderson, 1989). In addition, the Health Education Council in Britain recommends a daily dietary fiber intake of 30 grams (Trowell et al., 1985).

Renal patients on hemodialysis frequently suffer from complications including constipation, diabetes, Type IV hyperlipidemia, and diverticulosis (Cochran, 1982; Guarnieri et al., 1980; Levine, 1982; Zeman, 1983). Some of these complications may be related to compliance with necessary dietary modifications and/or prescribed medications (such as aluminum antacids). Inclusion of selected sources of dietary fiber has been shown in other patient populations to have positive effects on conditions including constipation, diabetes, hyperlipidemias, and some gastrointestinal tract disturbances (Anderson, 1979; 1985; 1987;

Andersson, 1979; Cummings, 1978; Kay, 1982; Jenkins, 1988; Simpoulos, 1986).

Constipation

Constipation has been defined as "a chronic condition (> six weeks) characterized by hard stools or fewer than three bowel movements per week" (Ross Laboratories, 1990). Constipation has also been stated as having the most meaning when viewed as "a change from an individual's customary bowel habits"; and it may refer to a reduction in frequency of defecation, a constant sensation of rectal fullness with incomplete evacuation of feces, or sometimes painful defecation due to hard stools or perianal pathology (Harrison, 1983; Taylor, 1990; Zeman, 1983). Constipation is a common complaint of hemodialysis patients. A survey of 16 dialysis units in Michigan revealed that 15 (93%) of the units consider constipation to be a problem in their population (Fischer and, Jones, 1991). A recent survey of patients using the Sparrow hospital hemodialysis unit (n=87) revealed that 66% of those patients surveyed experienced problems with constipation at least one to two times per week (Fischer, personal communication, 1990). Medications (e.g. aluminum antacids, antidepressants, and antihypertensives), fluid restriction, lack of exercise, potassium restriction (limiting intake of some fruits and vegetables), and phosphorus restriction (limiting intake of whole grain products) are among the causes of constipation in hemodialysis patients (Adams et al., 1982; Burgess et al., 1987; Chambers, 1983; Ghose, 1970; Hoover, 1989; Welch et al., 1980).

The use of fiber in the treatment of constipation and uncomplicated diverticular disease has been well established (Kay, 1982; Trowell et

al., 1985). Insoluble fibers, such as cellulose, have been shown to increase fecal bulk and decrease intestinal transit time (Anderson, 1986). Andersson et al. (1979) found that inclusion of 20 grams of coarse wheat bran in the diet of ten constipated geriatric patients decreased intestinal transit time significantly ($p<0.02$) in comparison to a bulk laxative preparation that the subjects were using originally.

Wrick et al. (1983) tested transit time in 24 males during an 80-day metabolic study using breads with four fiber sources and varying neutral detergent residue (NDR): (a) white wheat bran ground to coarse (13.6 g NDR) or fine particle size (12.8 g NDR), (b) purified cellulose (17.8 g NDR), (c) cabbage fiber (9.9 g NDR plus pectin), and (d) white bread which contained 1 gram NDR (control). Each subject received each treatment in a crossover design study. The investigators found that coarse bran and cellulose decreased transit time significantly ($p <0.05$). Grinding of the bran was found to decrease the fecal output due to reduced fecal water. However, it also was found that increased intake of all types of fiber linearly increased fecal output of water and dry matter. If fiber supplementation can act to reduce constipation in the renal patient on hemodialysis, and thus to normalize the bowel habits, it may increase both medication and diet compliance. If the hemodialysis patient is able to follow both the diet and medication regimens that are prescribed and still have no problems with bowel irregularity, he/she may be more likely to comply with these regimens.

Blood Glucose

Fiber supplementation may have an effect on blood glucose levels. Mechanisms of action of dietary fiber on carbohydrate metabolism may

vary. In short-term studies, the effect of fiber appears to be in the upper gut. In longer-term studies, the mechanisms of action of fiber on blood glucose may be due to metabolic changes in the upper gut as well as to fermentation in the lower gut (Wahlqvist, 1987).

Jenkins et al. (1975), documented in diabetic subjects that blood glucose and insulin responses were both lower after meals that were fiber supplemented than they were following fiber free meals. The responses were attributed, in part, to the ability of soluble fiber to impede intestinal absorption and to slow gastric emptying.

Anderson (1985), reported on the use of a high carbohydrate, high fiber diet (70% carbohydrate, 18% protein, 12% fat, and 70 grams of plant fiber) in a three week metabolic ward study with 25 lean type I diabetics. The amount of fiber added to the diets was well above the recommended 25-35 grams for the average adult. However, insulin needs decreased by 38%, fasting blood glucose levels decreased by 16%, and serum cholesterol levels decreased by 31% over the three weeks.

Parillo et al. (1988) found that incorporation of 50% carbohydrate by caloric density (equaling approximately 65 g of dietary fiber per day mostly of the vegetable or soluble-type fibers) into the diet of six insulin dependent diabetic patients with chronic renal failure over the course of a 10 day metabolic study resulted in a significant decrease in blood glucose levels ($p<0.05$). The data were compared to the those obtained following the traditional diabetic diet for patients with renal failure (reported to contain approximately 40% carbohydrate and 22 grams of dietary fiber).

Hamberg et al. (1989) studied the effects of the daily addition of pea fiber (30 grams), sugar beet fiber (22 grams), or wheat fiber

(36 grams) on postprandial blood glucose and serum insulin in eight healthy subjects. They reported that the pea fiber significantly reduced the postprandial blood glucose response ($p < 0.05$) while not significantly affecting the insulin response. Neither wheat fiber nor sugar beet fiber significantly altered any of the variables; however, they did decrease intestinal transit time ($p < 0.05$).

Blood Lipids

Fiber supplementation also may affect blood lipid levels. Soluble fiber may influence cholesterol and lipid metabolism at hepatic or peripheral sites (Anderson, 1987). deGroot et al. (1963) reported in a study with 21 males (age 30-50 years) that incorporation of 140 g of rolled oats into the regular diet in the form of 300 g of bread, over the course of three weeks, resulted in a 12% decrease in serum cholesterol levels.

Jenkins et al. reported in 1975 that incorporation of 36 g of guar gum or pectin into the diet of twelve males (age 21-32 years) over a period of two weeks caused the serum cholesterol levels to fall significantly (guar gum $p < 0.002$; pectin $p < 0.05$). Incorporation of 36 g of wheat fiber, however, did not affect blood cholesterol levels.

Hagander et al. (1989) compared a sugar beet enriched diet (27 g of dietary fiber) to that of a control diet in 12 non-insulin dependent diabetic patients in a 16 week cross-over study. The results revealed that the sugar beet fiber-enriched diet decreased systolic blood pressure ($p<0.05$), decreased total plasma cholesterol ($p <.05$), and increased levels of HDL-cholesterol ($p <0.05$). The sugar beet fiber-

enriched diet had no significant effect on fasting blood glucose levels, postprandial blood glucose levels, or glycosolated hemoglobin levels.

Fluid Allowance

Fiber supplementation may allow an increase in the daily allotment of fluid for the hemodialysis patient as some types of fiber have a high water holding capacity. This may have an effect on the dry weight (weight after a dialysis session) of the hemodialysis patient and/or on the interdialytic (between dialysis sessions) weight gain. This water holding capacity of some fibers may allow for increased excretion of water via the gastrointestinal tract (i.e. not filtered by the kidney) (Kay, 1982). Gums, pectins (found in sugar beet fiber and oat fiber), mucilages, and storage forms of polysaccharides have high affinities for water and swell to form gels in the small intestine in the presence of water. Cellulose (found in pea fiber and sugar beet fiber) can bind to approximately 0.4 g of water per gram of fiber in the intestinal tract (Anderson, 1979).

Other Blood Constituents

It has also been suggested that fiber may affect urea synthesis in the renal patient (Rampton et al., 1984). Yatzidis et al.(1979) reported in a study using two uremic patients that ingestion of locust bean gum (25 grams in three divided doses daily) over 19 weeks resulted in a decrease in serum creatinine, phosphorus, and urea. The authors suggested that these decreases were related to the capacity of the gum to adsorb urea, creatinine, uric acid, ammonia, and phosphorus in the intestinal lumen.

Minerals and Electrolytes

The use of high fiber foods, such as wheat bran, in the diet of renal patients has been controversial, as these foods are also high in potassium and phosphorus (Pennington and Church, 1986; Zeman and Nay, 1988).

Another concern associated with increasing dietary fiber is that hemodialysis patients often show signs of anemia and low levels of some minerals. Calcium, iron, and zinc have been shown to bind to dietary fiber (Southgate, 1987). However, evidence from studies done on the nutritional status of persons consuming high fiber diets suggests that the long-term effects of fiber on mineral absorption are negligible provided that the diet is adequate with respect to nutrients (AMA Council on Scientific Affairs,1989; Southgate, 1987; Toma et. al, 1986). Due to the complexity of the hemodialysis patient's diet and the common occurrence of anemia, it was important to determine if fiber supplementation complicated existing conditions and if key laboratory blood values (such as potassium, phosphorus, calcium, creatinine, blood urea nitrogen, iron, cholesterol, triglycerides, lipoproteins, glucose, and ferritin) remained within acceptable ranges.

Commercially Available Fiber Supplements

Several products are available on the market that are classified as fiber supplements and bulk forming laxatives to aid in the relief of constipation. Following is a review of some of these products.

Fiberall is made by CIBA and is marketed as a bulk-forming and non-irritant laxative. The active ingredient of *Fiberall* is a refined

hydrophilic mucilloid extracted from the seed husk of the blond psyllium seed (Plantago ovata). *Fiberall* contains psyllium hydrophilic mucilloid, citric acid, flavor, polysorbate 60, and wheat bran. It is recommended to be taken as one teaspoon in a glass of water (8 ounces), one to three times a day. Each teaspoon contains approximately 2.2 g of soluble fiber, < 10 mg of sodium, < 60 mg of potassium, and < 6 calories (Barnhart, 1990).

Unifiber is made by Dow B. Hickman, Inc. and is a powdered cellulose product. *Unifiber* contains powdered cellulose, corn syrup, and xanthan gum. This non-gelling product can be added to liquids or soft foods. A one tablespoon serving contains 3 grams of insoluble fiber, no sodium, and < 4 calories. The recommended dosage is one to two tablespoons once or twice per day (Barnhart, 1990).

Metamucil is made by Procter & Gamble and is a bulk forming natural fiber that has psyllium hydrophilic mucilloid as its active ingredient. Regular flavor *Metamucil* contains psyllium hydrophilic mucilloid and dextrose. It can be purchased in orange, lemon-lime, and strawberry flavors and in both regular and sugar-free varieties. A one teaspoon serving of regular flavor *Metamucil* contains approximately 2.2 g of soluble fiber, < 10 mg of sodium, 31 mg of potassium, and 14 calories. One teaspoon in eight ounces of water is recommended one to three times per day (Barnhart, 1990).

Citrucel is made by Lakeside Phamaceuticals and is a bulk forming fiber that has methylcellulose as its major active ingredient. *Citrucel* contains methylcellulose, citric acid, FD&C Yellow No. 6, orange flavors, potassium citrate, riboflavin, and sucrose. One 19 g serving (approximately one heaping tablespoon) of *Citrucel* contains 2 g of

methylcellulose, 60 calories, 3 mg of sodium, and 105 mg of potassium. The standard dose is one heaping tablespoon of the product in eight ounces of water taken one to three times per day (Barnhart, 1988).

Fibercon is made by Lederle Laboratories and is a bulk forming fiber laxative that is concentrated in a tablet form. The major active ingredient is calcium polycarbophil. *Fibercon* also contains magnesium stearate, microcrystalline cellulose, silica gel, stearic acid, and other ingredients. One tablet contains 625 mg of calcium polycabophil equivalent to 500 mg of polycarbophil. The recommended dose is two tablets with eight ounces of fluid one to four times a day (Barnhart, 1988).

Serutan is made by Beecham Products and is a natural fiber laxative that has psyllium as its major active ingredient. *Serutan* contains psyllium, dextrose, oat flour, silicon dioxide, wheat germ, and flavors. One heaping teaspoon contains 3.4 g of psyllium. The recommended dose is one teaspoon in eight ounces of water taken one to three times per day (Barnhart, 1988).

Correctol powder is made by Plough, Inc. and is natural grain laxative with fruit fiber that has psyllium hydrophilic mucilloid as its major active ingredient. *Correctol* powder contains psyllium hydrophilic mucilloid, apple fiber, bran, citric acid, D&C yellow No. 10 and 40, flavor, sodium saccharin, and other ingredients. One rounded teaspoon contains 3.5 g of psyllium hydrophilic mucilloid, < 10 calories, and < 0.01 g of sodium. One teaspoon in eight ounces of water taken one to three times per day is recommended (Barnhart, 1988).

Syllact is made by Wallace Laboratories and has powdered psyllium seed husks as its major active ingredient. *Syllact* also contains

powdered dextrose, potassium sorbate, methyl and propylparaben, citric acid, FD&C red No. 40, flavor (artificial), and saccharin sodium. One rounded teaspoon contains 3.3 g of powdered psyllium seed husks and 14 calories. The manufacturer recommends one rounded teaspoon with eight ounces of fluid one to three times per day (Barnhart, 1988).

Effer-Syllium is made by Stuart Pharmaceuticals and is a natural fiber-bulking agent that has psyllium hydrocolloid as its major active ingredient. *Effer-Syllium* also contains citric acid, ethyl vanillin, lemon and lime flavors, potassium bicarbonate, potassium citrate, saccharin calcium, starch, and sucrose. One rounded teaspoonful contains 3 g of psyllium hydrocolloid and < 5 mg of sodium. The recommended dosage is one rounded teaspoonful in a glass of water one to three times a day (Barnhart, 1988).

Fibrad, one of the most recent fiber supplements marketed, is produced and distributed by Ross Laboratories and is a nongelling, concentrated, dietary fiber supplement. *Fibrad* contains 75% pea fiber, 15% oat fiber, 10% sugar beet fiber, xanthan gum, and soy lecithin. Of the fibers listed in the ingredients, *Fibrad* contains insoluble fiber from peas and sugar beets. Soluble fiber is derived from peas, sugar beets, oats, and xanthan gum (Hamberg et al., 1989; Kelsay et al., 1978; McConnell et al., 1974; Michel et al., 1988; Slavin, 1987). *Fibrad* contains over 80% total dietary fiber by weight of which over 90% is insoluble. *Fibrad* has been analyzed by the AOAC Method and found to be 78.6% insoluble and 7.4% soluble fiber by weight (Prosky et al., 1988). When analyzed by the modified Theander method, *Fibrad* was found to contain 80% insoluble and 3.8% soluble fiber by weight (Theander, 1986; Marlett et al., 1985). The insoluble fraction of *Fibrad* was found to be

primarily cellulose, hemicellulose, and insoluble pectins. *Fibrad* is also low in sodium (< 15 mg per 9 gram serving) and potassium (< 15 mg per 9 gram serving) (Ross Laboratories, 1990).

Due to factors that restrict the intake of dietary fiber from ordinary food sources in the diet of the hemodialysis patient, the problem with constipation as reported in a survey of renal units in Michigan, and the lack of research in this area, the addition of a fiber supplement to the diet of hemodialysis patients was deemed to be an area open to much needed research.

CHAPTER III

METHODS AND PROCEDURES

This study was conducted to determine the benefits and disadvantages of adding fiber to the diet of a population of hemodialysis patients. Basic methods involved in this research study included: development of a suitable product for incorporating fiber into the diet of the population; development of the forms and questionnaires to be used; subject selection; conduction of study; tabulation and statistical analysis of collected data. The following chapter explains in detail the steps in the research process used to reach this objective.

Study Approval

Approval to conduct this study was obtained from the University Committee on Research Involving Human Subjects (UCRIHS) at Michigan State University and from the Sparrow Hospital Institutional Research and Review Committee (Appendix 1) prior to the study via phone, and confirmed by letter. Each subject was informed of the purpose of the study and the need for his/her participation. Subjects were informed as to the necessity for access to their medical records for information on previous medical history, laboratory values, medication records, and

dialysis schedules. Those agreeing to participate signed a consent form (Appendix 1).

Sample and Subject Selection

Twenty-two subjects were recruited from a population of hemodialysis outpatients from Sparrow Hospital, located in Lansing, Michigan. Subjects who met the following criteria and indicated willingness to participate were selected. Criteria for selection included:

1. Had been on hemodialysis for at least 2 months.
2. Had maintained a serum potassium and phosphorus concentration between 3.0 and 6.5 mEq/l and 3.5-6.5 mg/dl, respectively, for two months prior to the study (relates compliance with diet and/or medication orders).
3. Had no physical and/or mental complications which interfered with or would have been aggravated by participation in the study.
4. Had permission from his/her nephrologist to participate in the study.
5. Had no known allergies to any ingredients in the fiber supplement.
6. Were approved by renal dietitian as to probability of compliance with study format.

Research Site

The study was conducted through Michigan State University in collaboration with the hemodialysis unit at Sparrow Hospital. The actual study was conducted at the hemodialysis outpatient unit at Sparrow Hospital in Lansing, Michigan. The fiber supplement (experimental) cookie was developed in the sensory lab at Michigan State University. The preparation of the experimental fiber supplement and control sugar cookies took place both at Michigan State University (Food Science Rm 124) and the kitchen facilities at Sparrow Hospital.

Research Design

At the initiation of the study each of the 22 subjects was randomly and evenly assigned to one of two treatment groups (A or B). This was done by placing slips of either white or green paper in unmarked sealed envelopes and having the subjects select an envelope from a box that contained all of the envelopes. The white slips of paper corresponded to the selection of being in group A, while the green paper slips corresponded to group B. Both groups received both treatments during the 57 day study, which used a cross-over design. The random assignment to a specific group served to indicate which group started with which treatment. Group A started with the control (plain sugar cookie group) treatment, and group B the experimental (fiber supplement cookie group) treatment. The independent variable in this study was the treatment with either fiber supplement cookies (containing Fibrad) or control (plain sugar) cookies. Each subject served as his/her own control in

this blind cross-over design. Distribution of study materials, collection and review of completed forms, and routine medical testing of the subjects took place during each subject's specified dialysis period within the dialysis unit.

Timeline

The study, conducted between October 22 and December 18, 1990, was composed of two baseline periods of one (1) week each and two treatment periods of three (3) weeks each. The baseline periods (no treatment) were at the beginning of the study and between the two treatment periods.

The sequence of the study is listed in Table 3.1 below.

Table 3.1 Sequence of study

	Period I week 1	Period II weeks 2-4	Period III week 5	Period IV weeks 6-8	Day 57
Group A	Baseline	Control Cookies	Baseline	Fiber Cookies	Summary
Group B	Baseline	Fiber Cookies	Baseline	Control Cookies	Summary

Data Collection

Blood Sampling

Each subject had fasting blood samples taken on day 1 of Periods II, III, and IV, and day 57 of the study prior to the subject's dialysis

session if he/she was on a morning dialysis schedule. If the subject was on an afternoon dialysis schedule, the subject came to the hospital in the morning of the day the blood sample was to be drawn (See daily schedule for subjects in Appendix 2). The study was started on the subjects' normal day of dialysis (either Monday, October 22, or Tuesday, October 23, 1990). The 15ml blood samples were drawn by Sparrow Hospital laboratory personnel, and processed by the laboratory technician per hospital protocol. The samples were sent to Life Chem Laboratory in Northvale, New Jersey. This laboratory was selected because it is the laboratory which routinely analyzes the Sparrow Hemodialysis Unit samples. LifeChem uses both internal and external quality control programs in an effort to assure consistently reliable laboratory results. Internal quality controls are performed daily using both assayed and unassayed materials obtained from commercial sources. External monitoring of laboratory performance is achieved through participation in laboratory survey programs conducted by the College of American Pathologists and the New Jersey State Health and Environment Department.

Dietary Data Collection

Dietary data were collected using food records for three days during periods I, II, III, and IV of the study; each subject kept a complete food and liquid intake record for three days (one dialysis, one non-dialysis, and one weekend). This record consisted of a listing of all foods and liquids that the subject had consumed in that 24 hour period. Each subject was given a set of standard measuring spoons and measuring cups, and was instructed on the use of basic household

measurements and standard portion sizes by either Diane Fischer, M.S., R.D.(renal dietitian), or Marci Askegard, R.D. (graduate research assistant) for accuracy in reporting amounts consumed. The instruction was given at the beginning of the study (day 1 of period I). Each food record was reviewed for completeness by the dietitian working with the subject at the time that records were returned to the research staff, and any missing information was obtained from the subject.

Study Forms

Subjects were asked to complete several forms (e.g. background information, general condition, and product tolerance/acceptance) during specific days of the study. Each subject also kept a daily record of medications taken during the study. Subjects received instruction on completion of these forms during day 1 of period I. Each subject received a daily checklist and a packet of forms at the beginning of each week during the study. The subject received a three ring binder notebook to hold the forms, and was instructed to bring the notebook to the dialysis unit at the beginning of each week during the study. A packet of completed forms was turned in to the renal dietitian (Diane Fischer, M.S., R.D.) or graduate research assistant (Marci Askegard, R.D.) at the beginning of each week, starting with week two (2) of the study. Forms were checked by either the renal dietitian (Diane Fischer, M.S., R.D.) or the graduate research assistant (Marci Askegard, R.D.) to assure that each had been completed. Medical records were used to get information including patient weight and between session weight gain. The subjects were weighed at the beginning and at the conclusion of their dialysis sessions on a Scale-Tronix digital scale as per normal

Sparrow Hospital Dialysis Unit protocol. The scale used to weigh the hemodialysis subjects is accurate to .10 pounds and is checked for accuracy on a daily basis by the nursing staff on the outpatient hemodialysis unit.

A complete description of the daily schedule of subject activities for the study including form completion can be found in Appendix 2. Form A (Appendix 3) covered basic background information about the bowel habits, diet, and possible prior problems with constipation that a subject may have experienced. Form B (Appendix 4) contained general condition questions related to bowel movement frequency and gastrointestinal problems. Form C (Appendix 5) contained questions dealing with the acceptability of the product (i.e. fiber cookies, or plain sugar cookies). Form D (Appendix 6) was a rank evaluation of the product's qualities in such areas as appearance, color, flavor, taste, and texture. Form E (Appendix 7) was a food/liquid intake record for a 24 hour period. Form F (Appendix 8) was designed for obtaining the daily medication schedule of each subject. Form G (Appendix 9) was designed for obtaining the daily consumption of cookies during the treatment periods. The subjects in the study completed the appropriate forms as listed in the research design. Form H (Appendix 10) was designed for use by the student assistant (Patrick Kennedy) who abstracted the subject's medical records. Form I (Appendix 11) was designed as a follow-up tool to evaluate the study based on subject reaction and comments.

Forms A, B, C, and D, are adaptations of forms used in previous studies. Adaptations were based on the special needs/conditions of the renal hemodialysis patient, and on the proposed purpose and hypotheses

of this study. These forms were reviewed by an expert panel of six persons for face and construct validity. Form E was a modification of a form developed by Dr. Jenny Bond (investigator) in a prior study. Forms F, G, and I were developed by Marci Askegard, R.D.(graduate research assistant) and Dr. Bond for specific use in this study. Form H was developed by Patrick Kennedy (student assistant), who worked with the gathering of the information from the medical charts. Forms E, F, G, H, and I were reviewed by an expert panel. Forms were color coded according to week and group to facilitate their appropriate use by subjects. Each form had a blank for recording the subject number at the top portion of the form. These numbers were used for identification during the tabulation of the data. Each form was also identified by a removable name label. Each subject had his/her name on this label for ease in distribution of forms. Each subject was instructed to write his/her given number on all forms. The name labels were removed prior to the analysis portion of the study to retain the anonymity factor for the subjects in the study.

Phone Interview

Subjects were contacted by phone six months after the end of the research study to determine if they could identify whether they had consumed fiber cookies during each treatment period. Subjects were asked two questions: " Could you tell which time you had the fiber cookies -- was it the first or second time you were on cookies? What was the difference you noticed between the two periods? "

Treatments

The experimental treatment consisted of approximately 14 grams of fiber supplemented (from Fibrad supplement). The subjects consumed two (2) cookies on day one of the treatment period, three (3) cookies on day two of the treatment period, and four (4) cookies per day for the remaining days of the treatment period. Consumption of four fiber supplement (4) cookies per day provided 14.52 grams of dietary fiber. When subjects consumed four control sugar cookies, approximately 0.96 gm of fiber was consumed.

If a subject was not able to tolerate the average of 14.52 grams of fiber, the subject was instructed to decrease intake to 3 cookies per day. It was not necessary for any subjects to withdraw from the study due to intolerance of the cookies. Subjects that used stool softeners prior to the start of the study and who could not discontinue them during the control period due to discomfort or medical reasons, were allowed to remain on the stool softeners for the duration of the study. Use of stool softeners by any subject was recorded and considered in evaluation of results.

Abstracting Medical Records

Information was abstracted from each subject's medical record by a trained student assistant. The student assistant (Patrick Kennedy) was trained and monitored by the renal dietitian (Diane Fischer, M.S., R.D.) in gathering information from the medical chart. The following data were obtained for each subject:

a. Total time on dialysis for each session.

b. Incidence of blood transfusion (if required)

c. Whether the subject "crashed" during dialysis; that is, did the subject 's blood pressure drop to the point that saline was given?

d. Height, weight, and between dialysis weight gain.

e. Age, diet prescription, diagnoses.

f. Other medical information which could affect the interpretation of the results of the study (e.g. illness).

All information taken from the medical record was recorded on Form H for each session that the subject was on dialysis, and a tally sheet was kept of the dialysis sessions. Interdialytic weight changes were calculated by subtracting the post-dialysis weight from the pre-dialysis weight of each subject at each dialysis session. The average weight change per subject was taken from differences in dry (post-dialysis) weights taken at each dialysis session. Individual subject weight data from dialysis sessions during each period were averaged to give one value for each subject during each period.

Cookie Preparation, Handling, and Composition

The experimental fiber supplement cookies and the control sugar cookies were prepared using standardized recipes (Appendix 13). The recipes for the control sugar cookie and the fiber supplement cookie were standardized by caloric content. The fiber amount per cookie was calculated on a per gram weight basis of the pre-baked cookie.
The standardization of the cookie recipes was completed by the graduate research assistant (Marci Askegard, R.D.) in the Sensory Laboratory

(Room 102 Food Science Building) prior to the beginning of the study periods. Preliminary testing for acceptance and palatability of the cookies was completed at Michigan State University by Food Science and Human Nutrition faculty and graduate students, and at Sparrow Hospital by outpatient hemodialysis patients and staff prior to the initiation of the study. The cookies used for the first four days of the first treatment period were made in the research laboratory kitchens in the Food Science Building (room 124G) at Michigan State University. The cookies for the remaining days of the first treatment period and for the second treatment period were made in the bakery at Sparrow Hospital. The cookies were made under the supervision of the graduate research assistant (Marci Askegard, R.D.) and the hospital chef (Don Benson) to ensure quality control. Ingredients used to prepare the cookies were bought in common lots from Michigan State University Food Stores or at Goodrich's, a local supermarket. All dry ingredients, egg substitute, and margarine were weighed on calibrated Mettler balances (4600 or PE16) to +/- 0.2 g (except for the baking soda and cream of tartar which was +/- 0.1 g). The liquids were measured in graduated cylinders to +/- 1.0 ml. Cookie ingredients were mixed according to directions (Appendix 12). The cookie dough was measured, and each dough ball was weighed on a Mettler or spring loaded balance. Each control sugar cookie was weighed to a prebaked weight of 30 grams +/- 1.0 gram. Each experimental fiber supplement cookie was weighed to a prebaked weight of 33.83 grams +/- 1.0 gram. Each ball of cookie dough was placed on an individual square of parchment paper and placed on a cookie sheet for baking. The cookies made at Michigan State University were baked in a National rotary oven with 6 racks at 325 degrees Fahrenheit . The

control sugar cookies were baked for 11-12 minutes, while the experimental fiber supplement cookies were baked for 14 minutes. The cookies made at Sparrow Hospital were baked in a Middleby Marshall Oven Company rotating oven at 325 degrees Fahrenheit. The control sugar cookies baked for 11 minutes, while the experimental fiber supplement cookies were baked for 14 minutes. The cookies were cooled on wire racks and transferred to packages of 15 or 30 cookies that were foil wrapped and labeled with either A or B. The letter A corresponded to the control sugar cookies and the letter B corresponded to the experimental fiber supplement cookies. Each foil wrapped package of cookies was placed in a zipper locked plastic bag to retain freshness during storage. All cookies were stored at 10 degrees Fahrenheit in Room 124 of the Food Science Building at Michigan State University. The subjects were given instructions for at home storage of the cookies, to maintain the quality of the product. The approximate composition of the cookies with respect to calories and dietary fiber is listed in Table 3.2.

Table 3.2 Calculated individual cookie composition[a]

Nutrient	Control Cookie (A)	Fiber Cookie (B)
Weight of Cookie (gm)[b]	30.0	33.8
Energy (kcal)	127.0	126.0
Protein (gm)	1.64	1.24
Fat (gm)	6.83	7.13
Carbohydrate (gm)	14.9	13.8
Potassium (mg)	26.0	30.4
Phosphorus (mg)	13.6	12.7
Calcium (mg)	8.02	7.71
Iron (mg)	0.51	0.33
Cholesterol (mg)	0.10	0.10
Water (gm)	6.76	7.14
Dietary fiber (gm)	0.24	3.63[c]

[a]Data obtained using Food Processor II Nutrition and Diet Analysis System (ESHA Research Inc., Salem, Oregon, 1988) for recipe analysis, and Fibrad data from Ross Laboratories.
[b]Weight of cookie before baking.
[c]3.5 grams from Fibrad.

Prior to the first treatment period (Period II), each subject received a four day supply of either A or B cookies. Each subject received a ten day supply of cookies on day 5 of the first week of Period II (week 2) . For the remainder of Period II and for Period IV, the subjects were given a seven day supply of cookies (i.e. 30 cookies) each week. Each subject returned the unused portion of cookies at the end of each one week period. These were counted and recorded as a check on actual cookie consumption.

Cookie Consumption

The subjects were instructed to consume two (2) cookies on day 1 of each treatment period, three (3) cookies on day two of the treatment

Evaluation of Study Acceptance

Subjects received a letter of appreciation for participation in the study and were asked to complete a return by mail study evaluation form for investigators (dated 3-20-91).

Analysis of the Data

Diet Record Analysis

Prior to any analysis of the diet records, Dr. Jenny Bond (investigator), and Marci Askegard (graduate research assistant) attended a two-day training session at the University of Minnesota to learn the procedure for entering the diet records into the Minnesota Nutrient Data System Entry Program. All diet records were coded by a trained graduate research assistant (Marci Askegard, R.D.), and double checked for accuracy by a trained undergraduate assistant (Susan Miller). The diet records were entered into the Minnesota Nutrient Data System Data Entry Program (NDS version 2.2) by the graduate research assistant (Marci Askegard, R.D.) and these entries were double checked by the undergraduate assistant (Susan Miller). Only three (3) foods on subjects' food records were missing from the data base. These were coded into the data base using foods with similar composition after consultation with the staff at the University of Minnesota. The computer discs containing diet data were then sent to the University of Minnesota and were analyzed using the Minnesota Nutrition Data System (NDS version 2.2). The data files that were sent back to Michigan State

University were loaded into SPSS/PC+ 4.0 for statistical analysis using a series of paired t-tests for baseline, control treatment, and fiber treatment periods. In this study intakes of energy (kilocalories), total protein (gm), total fat (gm), total carbohydrate (gm), potassium (mg), phosphorus (mg), calcium (mg), iron (mg), sodium (mg), cholesterol (mg), water (gm), total dietary fiber (gm), water soluble fiber (gm), water insoluble fiber (gm), and pectins (gm) were determined. Intake was averaged for each of the four periods (i.e. for the three days of each of periods I, II, III, and IV). The three day averages of the subjects were pooled for comparison of the individual nutrients by period and treatment.

Blood Analysis

The fasting blood samples were sent to Life Chem Laboratories in Northvale, New Jersey for analysis. Chem 20 (serum blood test, with 20 tests), CBC (Complete Blood Count), and lipoprotein analysis reports were obtained. (A sample of these reports can be found in Appendix 14.) CBC analyses were not included as part of this particular study. Ferritin was determined initially (day 1 of period I), and after the treatment period in which the subject received the Fibrad fiber cookie (B) treatment. Important to this study were the serum values for blood urea nitrogen, creatinine, potassium, calcium, phosphorus, glucose, cholesterol, triglyceride, iron, high density lipoprotein, and ferritin. Statistical tests were performed on the tabulated values by the Biostatistics department at Ross Laboratories to determine if there were any differences in blood values by period and treatment. Ferritin values were analyzed by the graduate research assistant (Marci Askegard,

R.D.) using SPSS/PC+ 4.0 paired t-test to compare baseline values with those taken after the fiber treatment period.

Data From Completed Forms

Data from the series of completed forms (not including the food and beverage records) were compiled onto data flow sheets by the graduate research assistant (Marci Askegard, R.D.), and double checked by the undergraduate assistant (Susan Miller). Data were compiled for the following forms: background information (Form A), general condition (Form B), cookie acceptance (Form C), cookie evaluation (Form D), medication (Form F), cookie consumption (Form G), medical information (Form H), and the study evaluation form (Form I).

The data compiled from the background information form (Form A) were analyzed using basic descriptive statistics by the graduate research assistant. The data flow sheets compiled from the general condition form (Form B), the cookie acceptance form (Form C), the cookie evaluation form (Form D), the cookie consumption form (Form G), and the medical information form (Form H) were sent to Ross Laboratories for analysis by their biostatistics department. The graduate research assistant (Marci Askegard, R.D.) and advisor (Dr. Jenny Bond) checked all records submitted and analyses returned for completeness and accuracy.

The data compiled from the medication form (Form F) were compiled in Table 4.17 by the graduate research assistant for presentation and discussion in chapters IV and V. The information gathered from the study evaluation form (Form I) was tallied in chapter IV and discussed in

chapter V in relation to the subject's retrospective interpretation of the study.

Analysis of Data in Relation to Hypotheses

In the analysis of the data, baseline periods were compared to treatment periods of either fiber supplement cookie or control cookie for all dependent variables.

The subject's responses obtained from Form G (cookie consumption record) were used to determine compliance to the treatment regimen during the treatment periods of the study (Periods II and IV). Data from subjects that fell below the criteria of consumption of at least 3 cookies per day during the treatment period that contained the fiber cookies were omitted from the final results, The subject's responses obtained on Form B (general condition form), Form C (cookie acceptance form), and follow-up phone questions were used to determine if the fiber supplement was effective in treating or preventing constipation; and if there were any associated adverse effects on the gastrointestinal system of this population of subjects (Hypotheses 1, and 2).

Results from analysis of the diet records, and responses on Form C (cookie acceptance form) were used to determine if there was any decrease in food intake (Hypothesis 3).

The results from the analysis of the fasting blood samples and diet records were used to determine if the fiber cookie had any effect on serum concentrations of blood urea nitrogen, creatinine, potassium, phosphorus, calcium, glucose, cholesterol, triglyceride, iron, high density lipoprotein, or ferritin (Hypothesis 4).

Values from Forms C (cookie acceptance form) and D (cookie evaluation form) were used to determine acceptability of the fiber supplement product (Hypothesis 5).

The record of each subject's between-dialysis weight gain during treatment, data on dry weight changes, and diet record data on total water consumed were compared with and without the fiber supplement cookie. These data were used to determine if there was an effect of treatment on the dry weights and interdialytic weight gains of the renal hemodialysis subjects (Secondary Hypothesis 1).

The food intake records, combined with the medication intake records of all subjects, were compared for the two treatments [fiber supplement (B) or control (A) cookies]. These results helped to determine the effect of fiber supplementation on the adherence to diet prescription and medication orders of the renal hemodialysis patient (Secondary Hypothesis 2).

All parametric data were analyzed using crossover design Analysis of Variance (ANOVA) or paired t-tests. Data that did not meet the distribution assumptions of ANOVA or paired t-tests were analyzed by appropriate nonparametric statistical techniques (including descriptive statistics, frequencies, percent affected, and percent affected by subject day).

CHAPTER IV

RESULTS

The purpose of this study was to determine what the effects of addition of an insoluble fiber supplement product to the diet of a population of outpatient hemodialysis patients would be in relation to a number of dependent variables. The results of the analysis of data from the forms that were completed during the study [background information (Form A), general condition (Form B), cookie acceptance (Form C), cookie evaluation (Form D), daily record of consumption of food and beverages (Form E), medication (Form F), cookie consumption (Form G), and medical information (Form H)]; fasting blood samples; and follow-up study evaluation questionnaire (Form I) are reported and discussed in this chapter.

Sample Selection

The study began with twenty-two (22) chronic hemodialysis patients taken from a population of hemodialysis patients at Sparrow Hospital, located in Lansing, Michigan. The subjects were chosen from a pool of those patients who met previously stated criteria. Two subjects withdrew from the study during the first week, and two subjects withdrew during the second week. Two of the subjects were unable to complete the forms that were to be kept on a daily basis. Another subject decided the

study would interfere with his daily activities to a greater degree than he could handle. The other subject perceived that the control cookie had an undesirable side effect of diarrhea. The dropout rate for the study was 18%, which gave a study completion rate of 82% of those subjects beginning the study. The study completion rate after the first two weeks was 100%. Of the 18 subjects that completed the study, three (3) subjects had their data omitted from the final analysis due to noncompliance with the criteria of consuming at least three cookies per day during the fiber treatment period. Reasons for reduced consumption of cookies for two subjects was due to illness not related to the study, resulting in decreased or omitted days of cookie consumption during the treatment period. The third subject stated small appetite, and recorded five missed days of cookie consumption during the treatment period. This gave a usable data rate of 68% of those starting the study.

Initially the 22 subjects were placed randomly into two groups (A and B) of equal numbers. The 15 subjects that completed the study and had data that met the criteria for analysis gave a distribution of six (6) subjects in group A, and nine (9) subjects in group B. Subjects in group A were started on the control sugar cookie treatment, while subjects in group B were started on the experimental fiber supplement cookie treatment in the crossover design study.

Demographic Data

The 15 subjects consisted of five (5) females (33.3 % of study population) and ten (10) males (66.6 % of study population) ranging in age from 34 to 77 years. The mean age was 47.8 years.

The subjects had all been on hemodialysis for at least two months. The medical diagnoses that were at least in part responsible for the subjects' need for hemodialysis treatment are shown in Table 4.1.

Table 4.1 Subjects' medical diagnoses related to hemodialysis treatment[a]

Diagnosis	Percent of subjects (n)[b]
Nephritis	
Lupus	13.33 (2)
Chronic	6.67 (1)
Hypertensive glomerulo-	26.67 (4)
Tubulo-interstitial	6.67 (1)
Hypertension	13.33 (2)
Nephrosclerosis	13.33 (2)
Obstructive Uropathy	6.67 (1)
Renal Cancer	6.67 (1)
Acute Renal Failure (Septicemia)	6.67 (1)

[a]Data from Form H, (n=15).
[b]Percent of subjects with this diagnosis (number of total subjects).

Eight subjects (53.33%) required hemodialysis due to some type of nephritis. Hypertension and nephrosclerosis each claimed two subjects (13.33% each). Obstructive uropathy, renal cancer, and acute renal failure induced by septicemia each led to one subject (6.67%) needing hemodialysis (Table 4.1).

Table 4.2 Assessment of selected aspects of subject mobility[a]

	% Yes (n)[b]	% No (n)
Able to walk freely without assistance	80 (12)	20 (3)
Participate in other forms of exercise besides walking	7 (1)	93 (14)

[a]Self-reported data from background information (Form A), n=15.
[b]Percent of total subjects (number).

The subjects reported on their ability to walk and exercise as a part of the background information gathered. Eighty percent of the subjects were able to walk without assistance. But, only 7% of the subjects reported participating in forms of exercise in addition to walking.

Table 4.3 Self-reported dietary restrictions of hemodialysis patients[a]

Type of Restriction	% Yes (n)[b]	% No (n)
Potassium	93 (14)	7 (1)
Sodium	87 (13)	13 (2)
Protein	67 (10)	33 (5)
Phosphorus	80 (12)	20 (3)
Fluid	67 (10)	33 (5)

[a]Self-reported data from background information (Form A), n=15..
[b]Percent of total subjects (number).

The hemodialysis population in the study had five main dietary restrictions (Table 4.3). They were restricted in the amount of potassium, sodium, protein, phosphorus, and fluid allowed in their diets. Ninety-three (93) percent of the subjects were restricted in the amount of potassium they could consume on a daily basis, 87% in the amount of sodium, 67% in the amount of protein, 80% in the amount of phosphorus, and 67% in the amount of fluid allowed. It should be noted this is self-reported data. All subjects had, at some point during their ongoing therapy, been counseled on all parameters of their diets.

Measurements Related to Constipation and Fiber at Study Initiation

Table 4.4 Conditions and medications related to constipation, and fiber awareness of hemodialysis patients at initiation of study[a]

	% Yes (n)[b]	% No (n)	% No Response (n)
Conditions			
Bowel Irregularity	53 (8)	47 (7)	
Increasingly Constipated	33 (5)	67 (10)	
Hemorrhoids	20 (3)	80 (12)	
Fiber in Diet			
Aware of Need	87 (13)	13 (2)	
Concerned about Increasing Intake	47 (7)	47 (7)	7 (1)
Medications			
Stool Softeners	27 (4)	73 (11)	
Laxatives	13 (2)	87 (13)	

[a]Self-reported data from background information (Form A), n=15.
[b]Percent of total subjects (number).

Data obtained from subjects at the initiation of the study on conditions related to constipation, medications related to constipation, and fiber awareness are shown in Table 4.4. Fifty-three percent (53%) of the subjects reported bowel irregularity, while 33% of the subjects had been becoming increasingly constipated, and 20% suffered from hemorrhoids. Eighty seven percent (87%) of the subjects were aware of the need for increased fiber in the diet, while 47% were concerned about increasing the intake of fiber in their own diets. Twenty-seven percent of the subjects had taken stool softeners in the past to relieve constipation.

The subjects reported on the frequency of constipation and diarrhea during the year previous to the study. Of the subjects reporting, 80% took laxatives infrequently or not at all, while 7% took laxatives once week, and 13% more than once per week (Table 4.5).

Table 4.5 Frequency of constipation and diarrhea in hemodialysis patients during the previous year[a]

	Never % (n)[b]	Infreq. % (n)	1/month % (n)	1/week % (n)	>1/week % (n)
Took laxative for constipation	40 (6)	40 (6)	0 (0)	7 (1)	13 (2)
Had diarrhea	40 (6)	40 (6)	0 (0)	13 (2)	7 (1)

[a]Self-reported data from background information (Form A), n=15.
[b]Percent of total subjects (number).

Data on diarrhea revealed that 40% of the subjects had not experienced diarrhea over the previous year, while 40% had it infrequently (less than 6 times). Thirteen percent of the subjects had diarrhea more than once per week, and 7% percent reported having diarrhea more than once per week while 13% had taken laxatives.

Table 4.6 Stool number and consistency reported by subjects at study initiation[a]

	<4/week % (n)[b]	4-7 % (n)	8-14 % (n)	>14 % (n)	No Response % (n)
Average number of stools	33 (5)	27 (4)	13 (2)	20 (3)	7 (1)
		Loose % (n)	Soft % (n)	Firm % (n)	Hard % (n)
Stool Consistency[c]		7 (1)	27 (4)	53 (8)	40 (6)

[a]Self-reported data from background information (Form A), n=15.
[b]Percent of total subjects (number).
[c]Subject could choose more than one answer.

Subjects reported on the number of stools per week ,and stool consistency at the initiation of the study. Thirty-three percent of the subjects reported having less than four stools per week, 27% had four to seven stools, 13% had eight to fourteen, and 20% had greater than fourteen stools per week. One of the subjects (7%) did not answer this question. Stool consistency as reported by the subjects showed that seven percent of the subjects described their stools as loose, 27% as soft, 53% as firm, and 40% as hard (Table 4.6).

Cookie Consumption and Evaluation

Table 4.7 Total period and average daily consumption of cookies[a]

Group	Overall Consumption		Average Daily Consumption	
	Period II Mean±SE	Period IV Mean±SE	Period II Mean±SE	Period IV Mean±SE
Group A[b]	77.50±2.19	76.33±2.53	3.69±0.10	3.63±0.12
Group B[c]	77.22±1.24	76.33±2.82	3.68±0.06	3.63±0.13

[a]Self-reported data from records (Form G), with check back results (periods II and IV), n=15.
[b]Control during period II and fiber treatment during period IV.
[c]Fiber treatment during period II and control during period IV.

Table 4.7 reports the overall and average daily cookie consumption of both groups of subjects over the course of both treatment periods. All subjects met the required criterion of consuming at least three cookies per day over the course of the treatment periods. The subjects in group A had a mean daily intake of 3.69 cookies during the control treatment period and 3.63 cookies during the fiber treatment period. The subjects in group B had a mean daily intake of 3.63 cookies during the control treatment period and 3.68 cookies during the fiber treatment period. There were no significant differences between Periods II and IV in total or average daily cookie consumption.

Table 4.8 Cookie evaluation results by treatment[a]

Variable	Control Cookie Mean ± SE	Fiber Cookie Mean ± SE
Flavor	5.42±0.24	5.23±0.24
Texture	5.75±0.26	5.25±0.26
Taste	5.17±0.22	4.61±0.22
Aftertaste	4.92±0.44	4.17±0.42
Ease to chew/swallow	5.89±0.34	5.00±0.34
Tolerate every day	4.83±0.44	4.89±0.44
Overall evaluation	5.75±0.20	5.42±0.20

[a]Evaluations are based on a hedonic scale from 1 (dislike it very much) to 7 (like it very much). Evaluations were taken at the end of each treatment (periods II and IV), n=15.

The subject evaluations of each cookie are listed in Table 4.8. The cookies were evaluated on the characteristics of flavor, texture, taste, aftertaste, ease to chew and swallow, able to tolerate every day, and overall evaluation. The form used (see Appendix D) was based on a hedonic scale ranging from a score of 1 (dislike it very much) to 7 (like it very much). On the characteristic of flavor the control cookie had a mean score of 5.42, whereas, the fiber cookie had a mean score of 5.23. For texture the control cookie had a mean score of 5.75 and the fiber cookie had a score of 5.25. On the characteristic of aftertaste the control had a mean score of 4.92 and the fiber cookie had a score of 4.17. In relation to ease to chew and swallow the mean scores for the control and fiber cookies were 5.89 and 5.00 respectively. On the characteristic of able to tolerate and take every day the mean score for

the control cookie was 4.83 and was 4.89 for the fiber cookie. The overall evaluation mean score for the control cookie was 5.75 and for the fiber cookie was 5.42. The crossover analysis of variance revealed no significant differences between the two types of cookies on any of the characteristics measured. Both cookies had mean scores ranging between 4 (neither like nor dislike) and 6 (like slightly) on all characteristics. Thus, the subjects accepted both types of cookies, and had no extreme aversions to any of the characteristics of the cookies.

Table 4.9 gives results of the effects of the cookie on food intake determined from the cookie acceptance form that subjects filled out at the end of each of the two treatment periods. The control cookie did not affect the appetite of 20% of the subjects(n=3), increased the appetite of seven percent (n=1), and decreased the appetite of 20% (n=3). The control cookie left seven percent of the subjects feeling hungry (n=1) and reportedly left 27% (n=4) of the subjects feeling filled up. The fiber cookie did not affect the appetite of 27% of the subjects (n=4); either improved or decreased the appetite of 13% (n=2); did not leave any of the subjects feeling hungry; and left 53% of the subjects (n=8) feeling filled up.

Table 4.9 Effects of cookie on food intake[a]

	Response			
	Control Cookie		Fiber Cookie	
Statement	% Yes(n)[b]	% No(n)	% Yes(n)	% No(n)
The cookie did not affect my appetite.	20 (3)	80 (12)	27 (4)	73 (11)
The cookie improved my appetite.	7 (1)	93 (14)	13 (2)	87 (13)
The cookie decreased my appetite.	20 (3)	80 (12)	13 (2)	87 (13)
The cookie left me hungry.	7 (1)	93 (14)	0 (0)	100 (15)
The cookie filled me up.	27 (4)	73 (11)	53 (8)	47 (7)

[a]From self reports at the end of each treatment (Periods II and IV), n=15.
[b]Percent of subjects (number).

Constipation, Diarrhea, Defecation, and Gastrointestinal Variables

Table 4.10 reports percent of subjects reporting constipation, diarrhea, and pain associated with defecation during each period based on total subject days in the study. Group A subjects received the control cookie during period II and the fiber cookie during period IV. Group B received fiber cookies during period II and control cookies during period IV.

Table 4.10 Daily report of constipation and diarrhea[a]

	Period I (%)[b]	Period II % (trt.)[c]	Period III (%)	Period IV % (trt.)
Constipation				
Group A (n=6)	4.76	5.56 (control)	4.76	2.44 (fiber)
Group B (n=9)	20.97	10.05 (fiber)	11.11	14.36 (control)
Diarrhea				
Group A (n=6)	7.14	3.17 (control)	2.38	4.88 (fiber)
Group B (n=9)	9.84	2.12 (fiber)	0.00	0.53 (control)

	No Pain		Some Pain		Much Pain	
	A(%)[d]	B(%)[e]	A(%)	B(%)	A(%)	B(%)
Defecation						
Period I	80.00	94.60	2.50	5.40	17.50	0.00
Period II	97.50	96.70	2.50	1.70	0.00	1.70
Period III	100.00	98.30	0.00	0.00	0.00	1.70
Period IV	100.00	97.10	0.00	1.70	0.00	1.20

[a]Self-reported on Form B, based on total subject days (56), n=15.
[b]Percent of subjects affected based on total patient days by group.
[c]Percent affected (treatment).
[d]Group A (n=6) total percent of subjects affected.
[e]Group B (n=9) total percent of subjects affected.

The constipation data reveal a trend if the ratio of treatment period over baseline period is computed. For group A there was a 17% increase in percentage of reported constipation from baseline (period I) to treatment (period II) when consuming the control cookies, and a 51% decrease in percentage of subjects reporting constipation from baseline (period III) to treatment (period IV) when consuming the fiber cookies. For group B there was a 48% decrease in percentage of subjects reporting constipation from baseline (period I) to treatment (period II) when consuming fiber cookies, and a 29% increase in percentage of subjects reporting constipation from baseline (period III) to treatment (period IV) when consuming control cookies.

The percentage of subjects reporting diarrhea during the four periods does not show a clear increase/decrease relationship when the same ratio of treatment period over baseline is computed. There does not appear to be a common trend in both groups with this variable. The control cookie appeared to decrease the diarrhea in group A and increase the diarrhea in group B, whereas the fiber cookie appeared to decrease the diarrhea in group B and increase the diarrhea in group A.

The data on pain associated with defecation is also reported in Table 4.10. Group A subjects (based on patient days) reporting no pain with defecation was 80% (period I), 97.5% (period II), 100% (period III), and 100% (period IV); some pain associated with defecation of 2.5% (period I and period II), and 0.0% (periods III and IV); and much pain associated with defecation of 17.5% (period I), and 0.0% (period II, III, and IV). Group B had percentage reporting no pain with defecation of 94.6% (period I), 96.7% (period II), 98.3% (period III), and 97.1% (period IV); some pain associated with defecation of 5.4% (period I),

1.7% (period II), 0.0% (period III), and 1.7% (period IV); and much pain with defecation of 0.0% (period I), 1.7% (period II and III), and 1.2% (period IV). No definite trends emerge from this data. It does appear that the fiber treatment decreased the pain associated with defecation for some subjects in group B.

Table 4.11 contains the data from the reported daily stool number and consistency of stools. The first part of the table lists the means and standard error of the mean for both average number of stools and stool consistency by group. The lower part of the chart gives the results from the tests conducted on this data. Both average number of stools, and stool consistency were tested for first order carry-over effects, treatment-by-period interactions, and direct treatment effects for a cross-over design of ANOVA. There was no statistically significant change in stool consistency between any of the periods. There was a statistically significant difference between the first and second baseline periods in average number of stools. This denotes a carry-over effect of the first treatment period into the baseline period following it. Due to this carry-over effect, the data from the second treatment period was questionable for use in analysis.

Table 4.11 Statistical results of daily average number of stools and stool consistency by group and treatment[a]

Group	Period I Mean ± SE	Period II Mean ± SE	Period III Mean ± SE	Period IV Mean ± SE
Average number				
Group A[b]	2.33±0.47	2.52±0.47	2.88±0.46	2.58±0.43
Group B[c]	1.02±0.22	1.21±0.20	1.08±0.21	1.14±0.19
Average stool consistency[d]				
Group A	4.19±0.45	3.75±0.14	3.88±0.15	4.03±0.25
Group B	4.45±0.48	4.56±0.41	5.02±0.56	4.97±0.44

Tests by Treatment	Baseline	Trt. x Period Interaction	Sequence	D[e]	P[f]	Period II T-Test
Average number of stools	0.018[g]	---	---	---	---	0.098
Average stool consistency	0.328	0.742	0.742	0.771	0.141	---

[a]Self-reported data from Form B (Appendix 4) for all 56 days of study, n=15.
[b]Group was control during period II and fiber during period IV (n=6).
[c]Group was fiber during period II and fiber during period IV (n=9).
[d]Scale for consistency.
[e]D=direct effect.
[f]P=period effect.
[g]Significance level of $p<0.05$. Baseline significance means carryover effect.

The first treatment period was analyzed with mean treatment values over mean baseline values (proportion y\x) using a t-test . There was no statistically significant difference between the fiber and control cookie treatment in average number of stools based on this analysis.

Table 4.12 reports results of percentage of subjects reporting gastrointestinal symptoms (by patient days) during the four periods of the study. In group A percent of subjects reporting no nausea was 83.3% (Period I), 85.7% (Period II), 83.3% (Period III),and 88.8% (Period IV); mild nausea was 16.7% (Period I), 12.7% (Period II), 9.5% (Period III), and 8.0% (Period IV); moderate nausea was 0.0% (Period I), 1.6% (Period II), 7.1% (Period III), and 3.2% (Period IV); and sustained and severe nausea was 0.0% (Period I), 2.4% (Period II), and 0.0% (Periods III and IV). In group B percent of subjects reporting no nausea was 98.4% (Period I), 94.7% (Period II), 95.2% (Period III), and 92.6% (Period IV); mild nausea was 0.0% (Period I), 3.7% (Period II), 4.8% (Period III), and 4.3% (Period IV); moderate nausea was 0.0% (Period I), 1.1% (Period II), 0.0% (Period III), and 3.2% (Period IV); and sustained and severe nausea was 1.6% (Period I), and 0.0% (Period II, III, and IV).

In group A the percent of subjects reporting no abdominal cramps was 95.2% (Period I), 99.2% (Period II), 95.2% (Period III), and 97.6% (Period IV); mild cramps was 4.8% (Period I and III), 0.0% (Period II), and 2.4% (Period IV); moderate cramps was 0.0% (Periods I, III, and IV), and 0.8% (Period II); and sustained and severe cramps was 0.0% for all periods. In group B the percent of subjects reporting no abdominal cramps was 95.2% (Period I), 80.4% (Period II), 96.8% (Period III), and

Table 4.12 Daily report of gastrointestinal symptoms[a]

Symptoms by Period	None A(%)[b]	None B(%)[c]	Mild A(%)	Mild B(%)	Moderate A(%)	Moderate B(%)	Sustained and Severe A(%)	Sustained and Severe B(%)
Nausea								
Period I	83.33	98.39	16.67	0.00	0.00	0.00	0.00	1.61
Period II	85.71	94.71	12.70	3.70	1.59	1.06	2.38	0.00
Period III	83.33	95.24	9.52	4.76	7.14	0.00	0.00	0.00
Period IV	88.80	92.55	8.00	4.26	3.20	3.19	0.00	0.00
Abdominal cramps								
Period I	95.24	95.16	4.76	1.61	0.00	3.23	0.00	0.00
Period II	99.21	80.42	0.00	14.81	0.79	3.17	0.00	0.53
Period III	95.24	96.83	4.76	0.00	0.00	1.59	0.00	1.59
Period IV	97.56	83.51	2.44	7.45	0.00	5.32	0.00	3.72

	None A(%)	None B(%)	Occasional A(%)	Occasional B(%)	More than Usual A(%)	More than Usual B(%)	Excessive A(%)	Excessive B(%)
Intestinal Rumbling								
Period I	54.76	70.97	35.70	11.29	9.52	17.74	0.00	0.00
Period II	49.20	64.55	41.27	19.05	9.52	12.17	0.00	3.70
Period III	64.29	63.49	26.19	25.40	9.52	11.11	0.00	0.00
Period IV	59.35	51.32	39.02	31.75	1.63	13.23	0.00	3.70
Intestinal Gas								
Period I	28.57	50.00	69.05	25.81	2.38	6.45	0.00	17.74
Period II	50.00	48.15	40.48	29.63	9.52	12.70	3.97	6.88
Period III	61.90	46.03	26.19	33.33	11.90	20.63	0.00	0.00
Period IV	60.98	39.15	28.46	34.39	10.57	20.63	0.00	5.82

[a]Self-reported from form B based on total subject days (56), n=15.
[b]Group A (n=6) total percent of subjects affected.
[c]Group B (n=9) total percent of subjects affected.

83.5% (Period IV); mild cramps was 1.6% (Period I), 14.8% (Period II), 0.0% (Period III), and 7.5% (Period IV); moderate cramps was 3.2% (Period I and II), 1.6% (Period III), and 5.3% (Period IV); and sustained and severe cramps was 0.0% (Period I), 0.5% (Period II), 1.6% (Period III), and 3.7% (Period IV).

In group A the percent of subjects reporting no intestinal rumbling was 54.8% (Period I), 49.2% (Period II), 64.3% (Period III), and 59.4% (Period IV); occasional rumbling was 35.7% (Period I), 41.3% (Period II), 26.2% (Period III), and 39% (Period IV); more than usual rumbling was 9.5% (Periods I, II, and III), and 1.6% (Period IV); and excessive rumbling was 0.0% for all four periods. In group B the percent of subjects reporting no intestinal rumbling was 80% (Period I), 64.6% (Period II), 63.5% (Period III), and 51.3% (Period IV); occasional rumbling was 11.3% (Period I), 19.1% (Period II), 25.4% (Period III), and 31.8% (Period IV); more than usual rumbling was 17.7% (Period I), 12.2% (Period II), 11.1% (Period III), and 13.2% (Period IV); and excessive rumbling was 0.0% (Periods I and III), and 3.7% (Periods II and IV).

In group A the percent of subjects reporting no intestinal gas was 28.6% (Period I), 50% (Period II), 62% (Period III), and 61% (Period IV); occasional intestinal gas was 69.1% (Period I), 40.5% (Period II), 26.2% (Period III), and 28.5% (Period IV); more than usual intestinal gas was 2.4% (Period I), 9.5% (Period II), 11.9% (Period III), and 10.6% (Period IV); excessive intestinal gas was 0.0% (Periods I, III, and IV), and 4.0% (Period II). In group B the percent of subjects reporting no intestinal gas was 50% (Period I), 48.2% (Period II), 46% (Period III), and 39.2% (Period IV); occasional intestinal gas was 25.8%

(Period I), 29.6% (Period II), 33.3% (Period III), and 34.4% (Period IV); more than usual intestinal gas was 6.5% (Period I), 12.7% (Period II), 20.6% (Period III and IV); and excessive intestinal gas was 17.7% (Period I), 6.9% (Period II), 0.0% (Period III), and 5.8% (Period IV).

Nausea did not appear to be a problem with either group during either treatment. Group B seemed to be somewhat more affected in reported abdominal cramping during both treatment periods as compared to the baseline periods. Group A did not appear to be adversely affected by either treatment in the abdominal cramping category. There was a small percentage increase for both groups (from baseline) for intestinal rumbling with both treatments. There was not a consistent change in reports of intestinal gas by either group during the treatment periods.

Effect of Cookies on Laxation

Table 4.13 Subjects reports of effect of cookie on laxation[a]

	Response			
	Control Cookie		Fiber Cookie	
Statement	% Yes(n)[b]	% No(n)	% Yes(n)	% No(n)
The cookie made my bowel movements more regular.	47 (7)	53 (8)	60 (9)	40 (6)
The cookie made my bowel movements less regular.	13 (2)	87 (13)	27 (4)	73 (11)
The cookie made my bowel movements more comfortable.	53 (8)	47 (7)	60 (9)	40 (6)
The cookie is convenient to take any time of the day.	80 (12)	20 (3)	93 (14)	7 (1)
The cookie is as effective as other laxatives I have used.	40 (6)	60 (9)	53 (8)	47 (7)
The cookie is more effective than other laxatives I have used.	7 (1)	93 (14)	33 (5)	67 (10)
The cookie is more convenient than other laxatives I have used.	33 (5)	67 (10)	33 (5)	67 (10)

[a]From self reports at the end of each treatment (Periods II and IV), n=15.
[b]Percent of subjects (number).

The control cookie made bowel movements more regular for 47% of subjects (n=7), less regular in 13% (n=2), and made bowel movements more comfortable in 53% of subjects(n=8). The fiber cookie reportedly made bowel movements more regular in 60% of subjects (n=9), less regular in 27% (n=4), and bowel movements more comfortable in 60% of subjects (n=9)(Table 4.13).

Eighty percent (n=12) of control cookie subjects said the cookie was convenient to take any time of the day, whereas 93% (n=14) of subjects said the same about the fiber cookie.

Forty percent (n=6) of control subjects reported that the control cookie worked as effectively as a laxative, seven percent (n=1) reported it working better than a laxative, and 33% (n=5) reported it was more convenient than a laxative. Fifty-three percent (n=8) of subjects reported the fiber cookie as working as effectively as a laxative, 33% (n=5) as working better than a laxative, and 33% (n=5) as being more convenient than a laxative.

Subjects were contacted by phone for two follow-up questions six months after the study was conducted. The responses to the first question are listed in Table 4.14. Of the twelve subjects that were able to be contacted by phone, eight (66.7%) correctly identified the period during which they had the fiber cookies. One subject (8.3%) selected the control cookie period as being the fiber cookie period. In addition two subject (16.7%) stated they could not tell a difference in the cookies, and one subject (8.3%) could not remember which treatment period cookies were different.

Table 4.14 Subjects' identification of treatments [a]

Question	" Could you tell which time you had the fiber cookies -- was it the first or second time you were on the cookies? "			
	Correct	Incorrect	No Difference	Can't Recall
Responses	66.7 (8)[b]	8.3 (1)	16.7 (2)	8.3 (1)

[a]Follow-up done 6 months after study conducted, n=12.
[b]Percent of total responding (number of subjects).

Table 4.15 gives the responses of the subjects to the second question asked during the follow-up phone interview. The comments from the eight subjects that correctly selected the fiber treatment even six months after the study was conducted are shown in the top part of the table. The comments ranged from the cookie having a different texture and taste, to references of more regular and frequent bowel movements, and differences in the consistency of the stools that made them easier or more comfortable to pass.

The person that incorrectly selected the sugar cookie control treatment as the fiber treatment commented that the particular treatment had resulted in more bowel movements and more gas. Two subjects commented that they could detect no difference in the two treatments and one subject commented that although there had been a difference noted at the time of the study, it could not be recalled at this time.

Table 4.15 Differences reported by subjects related to treatments[a]

Question	" What was the difference you noticed between the two periods? "
	Comments
Correctly Identified Fiber Period	
Subject A[b]	"The cookie had a different texture, and made my stools easier to pass."
Subject B	"Tasted different, worked better, gave a looser stool that was easier to defecate."
Subject C	"Made bowel movements softer."
Subject D	"Made bowel movements more regular."
Subject E	"I wasn't bound up on that set of cookies."
Subject F	"They had a grainier texture, and made stools more comfortable to pass."
Subject G	"Bowel movements were fuller, firmer, and easier to pass."
Subject H	"Noticed change in bowel habits, I went more often."
Incorrectly Identified Fiber Period	
Subject I	"Had more bowel movements, and more gas."
Other Responses	
Subject J	"I couldn't really tell the difference."
Subject K	"I didn't detect any difference."
Subject L	"I did notice a difference back then, but I can,t remember now."

[a]Follow-up questions 6 months after study, n=12.
[b]Assignment of letters to subjects denotes no specific ordering of subjects or responses.

Average Dry Weight and Interdialyltic Weight Data

Table 4.16 Results for average dry weight and interdialytic weight change data[a]

Group	Period I Mean ± SE	Period II Mean ± SE	Period III Mean ± SE	Period IV Mean± SE
Dry Weight (lbs.)*				
Group A[b]	173.71±12.27	173.98±12.34	174.26±12.56	174.20±12.23
Group B[c]	148.60±12.51	149.33±12.54	149.92±12.64	150.48±12.55
Interdialytic ** Weight Gain (lbs.)				
Group A	6.61±0.66	6.50±0.70	6.38±1.21	5.98±1.21
Group B	4.03±0.67	5.09±0.40	4.19±0.75	5.04±0.46

[a]Data taken from medical record and based on weekly dialysis sessions, n=15.
[b]This group had control during period II, and fiber during period IV.
[c]This group had fiber during period II, and control during period IV.
*Treatment-by-period interaction p=.0001.
**Treatment-by-period interaction p=.0087.

Table 4.16 reports data on the average dry weight and interdialytic weight gains for subjects in each group (A and B) during each period throughout the study. Statistical tests were run for first order carry-over effects (changes between baseline period values), treatment by period interaction, and direct treatment effect. A significant treatment-by-period interaction was found for both the average dry weight and interdialytic weight between the two groups. This may have been due to the large difference in the initial weights of the two groups, and the response of the two groups not being consistent over the study period time. When comparing the two treatments (taking the treatment-by period interaction into account), there were no significant

differences found for either average weight dry weight or interdialytic weight change.

Blood Constituents

Table 4.17 includes the results from analysis of the fasting blood sample data. Four fasting blood samples from each subject were analyzed for first order carryover effects, treatment-by-period interactions, and direct treatment effect using a analysis of variance for crossover design studies. Ferritin blood values were analyzed using a paired t-test as there were only two samples drawn (baseline and after the fiber treatment). Results reveal that there was not a significant difference between periods for most of the biochemical constituents analyzed. There was a significant direct treatment effect for serum potassium at $p=0.015$. The serum potassium was significantly higher during the control treatment period than with the fiber treatment, but within the normal range. There is also a significant difference in the calcium blood values at $p=0.017$. Calcium levels were significantly higher in the control treatment period than with the fiber treatment, but again both remained within the normal range.

Table 4.17 Selected biochemical analysis of blood samples from fasting subjects[a]

Constituent (Reference Range)[b]	Baseline I Mean±SE	Control Mean±SE	Baseline II Mean±SE	Fiber Mean±SE
BUN (mg/dl) (6-19)	75.67±3.40	80.13±3.27	79.07±3.65	76.20±3.92
Creatinine (mg/dl) (0.8-1.6)	12.87±1.05	12.68±1.00	12.69±0.92	12.80±1.03
Potassium (mEq/l) (3.5-5.3)	5.22±0.23	5.21±0.16	4.89±0.14	4.99±0.16[c]
Calcium (mg/dl) (8.4-10.2)	9.14±0.17	9.19±0.17	9.07±0.18	8.91±0.17[c]
Phosphorus (mg/dl) (2.7-4.5)	6.03±0.30	5.85±0.39	6.54±0.34	6.18±0.37
Glucose (mg/dl) (70-105)	81.07±3.19	85.40±2.30	88.53±5.33	85.27±1.70
Total Cholesterol (mg/dl) (< 150)	180.2±14.9	172.3±12.2	185.9±15.0	171.5±13.0
Triglyceride (mg/dl) (59-158)	123.3±12.7	142.7±17.5	129.0±12.8	129.2±14.9
HDL (mg/dl) Male	37.0±3.2	34.4±2.3	35.3±2.8	35.4±3.5
Female (>35 male, >45 female)	45.4±6.1	44.6±7.1	49.2±6.3	44.2±5.4
Iron (mcg/dl) (37-158)	80.00±16.70	85.80±15.75	76.26±11.80	81.81±14.29
Ferritin (mg/dl) (7-350)	561.00±236.33	---	---	624.20±258.50

[a]Analysis of SMAC or ferritin from subjects fasted ≥ 12 hours, n=15.
[b]Reference range for LifeChem Laboratories analyses.
[c]Significantly different from control (sugar cookie) treatment ($p<0.05$).

Nutrient Intake

Table 4.18 Nutrient intake of subjects by treatment[a]

Nutrient	Baseline[b] Mean ± SE	Control Mean ± SE	Fiber Mean ± SE
Energy (kcal)	1648±145	1951±144[c]	2060±155[c]
Protein (gm)	61±6	63±7	69±6
Fat (gm)	73±7	93±7[c]	99±8[c]
Carbohydrate (gm)	184±16	217±18[c]	220±17[c]
Potassium (mg)	1567±190	1565±152	1785±252
Phosphorus (mg)	802±81	764±82	916±101
Calcium (mg)	453±71	375±51	489±79[d]
Iron (mg)	9.5±0.9	11.0±0.9[c]	11.4±1.3
Sodium (mg)	3127±342	3188±282	3248±242
Cholesterol(mg)	267±34	263±44	279±40
Water (gm)	1235±125	1247±121	1218±123
Dietary fiber (gm)	10.7±1.3	10.7±1.1	22.8±1.4[c,d]
Water insoluble fiber (gm)	7.0±0.9	7.9±0.7	18.4±1.0[c,d]

[a]Grouped 3 day averages for each subject in each period, n=15.
[b]Combined baseline (periods I and III).
[c]Significantly different from baseline period ($p \leq 0.05$).
[d]Significantly different from control cookie treatment ($p \leq 0.05$).

The nutrient intake data appear in Table 4.18. There were no significant differences found between baseline, control, and fiber treatments for protein, potassium, phosphorus, sodium, cholesterol, and water. There were no significant differences found between baseline and control for dietary fiber, water insoluble fiber, and calcium (although calcium approached significance at p=0.068). There were significant differences found between the baseline and both treatments (fiber and control) for energy, total fat, and total carbohydrate. There were no significant differences found between the two treatments for energy, total fat, and total carbohydrate. There were also significant differences found with the fiber treatment as compared to control and baseline for dietary fiber and insoluble fiber. There were no significant differences between the control and baseline for dietary fiber and insoluble fiber. There was a significantly higher intake of calcium in the fiber treatment as compared to the control, but no difference in the fiber treatment as compared to the baseline. A significant difference was found between the intake of iron during the control treatment as compared to the baseline period, with the fiber treatment approaching significance in comparison with the baseline at (p=0.066), and no significant difference found between the control and fiber treatments. Although there was statistical significance and approaching statistical significance for the dietary intake values of iron during control and fiber treatment periods, the actual difference in intakes would not have a physiological or practical significance based on the length of the study and iron supplementation of most of this population.

Relationship of Subjects' Diet Restrictions to Reported Diet Intake

Table 4.19 lists the noncompliance of subjects during the study to the diet restrictions prescribed (from medical record data). Each subject had an individualized diet prescription based on his/her medical condition, serum values, and fluid status. These diet prescriptions were obtained from the medical charts. The diet prescriptions were compared with the actual intake of the selected nutrients from the analysis of the diet records for each subject. Noncompliance was defined as exceeding the level of nutrient if a restriction had been imposed. Not all subjects were restricted on all nutrients listed in Table 4.19, however, these are the nutrients that are commonly restricted in the diet of the hemodialysis patient. It can be seen that two subjects (13%) were noncompliant to the potassium restriction during at least one baseline and one treatment period during the study.

One subject (7%) was noncompliant to the sodium restriction during at least one baseline and one treatment period, and three subjects (20%) were noncompliant during all four periods of the study. One subject (7%) was noncompliant to the prescribed protein restriction during only the treatment periods, two subjects (13%) were noncompliant during at least one baseline and one treatment period, and four subjects (27%) were noncompliant during all four periods of the study. In all cases, the noncompliance was not explained by the consumption of the cookies. All subjects were compliant with the prescribed phosphorus and fluid restrictions throughout the entire study. Based on these results, the fiber supplement did not affect the subjects' compliance with their diet restrictions.

Table 4.19 Noncompliance to diet restrictions during study period[a]

Restriction	Baseline[b]	Treatment[c]	Baseline/Treatment[d]	All Periods
Potassium	0 (0)[e]	0 (0)	13 (2)	0 (0)
Sodium	0 (0)	0 (0)	7 (1)	20 (3)
Protein	0 (0)	7 (1)	13 (2)	27 (4)
Phosphorus	0 (0)	0 (0)	0 (0)	0 (0)
Fluid	0 (0)	0 (0)	0 (0)	0 (0)

[a]Comparison of diet record analysis with diet prescription, n=15.
[b]Noncompliance during only baseline periods.
[c]Noncompliance during only treatment periods.
[d]Noncompliance during at least one baseline and one treatment period.
[e]Percent of subjects (number).

Medication Data

Table 4.20 lists all medications taken by subjects during all periods as reported on Form F. Subjects were taking a variety of drug classes: phosphate binders, nutrient supplements (calcium, iron, vitamins, other minerals), antihypertensives, cardiac glycosides, analgesics, anticonvulsants, and others. The few cases where different dosages were required (except analgesics taken occasionally) are indicated. In only three cases were dosages different between periods: Peri-Colace, Os-Cal, and Tylenol (Table 4.20). Tylenol is an elective medication and the dosage used may reflect the subject's situation rather than the treatment. The laxative Peri-Colace was required by Subject 2 during both baseline periods and when on the sugar cookie; it was not required while on the fiber supplement.

Table 4.20 Medications taken by subjects and the effect of treatment on dosages required

Subject	Medication	Drug Class\Type
Subject 1	Alu-Caps	Phosphate Binder
	Iron	Iron Supplement
	Taberon	Mineral/Vitamin Supplement
Subject 2	Alu-Caps	Phosphate Binder
	Apresoline	Antihypertensive
	Excedrin	Analgesic
	Feosol Iron	Iron Supplement
	Nephrocaps	Mineral/Vitamin Supplement
	Peri-Colace[a]	Laxative
	Tenormin	Beta Blocker
Subject 3	Cipro	Lipid Lowering Drug
	Doxycycline	Tetracycline Antibiotic
	Inderal	Beta Blocker
	Kayexylate	Cation Exchange Resin
	Lanoxin	Digitalis
	Loniten	Antihypertensive Vasodilator
	Nephrocaps	Mineral/Vitamin Supplement
	Oyster Shell Calcium	Calcium Supplement
	Therogram	Vitamin with Iron Supplement
	Tylenol	Analgesic
	Theophylline	Bronchodilator
	Vitamin C	Vitamin Supplement
Subject 4	Bumex	Loop Diuretic
	Cardene	Calcium Channel Blocker
	Ferrous Sulfate	Iron Supplement
	Nephrocaps	Mineral/Vitamin Supplement
	Normodyne	Beta Blocker
	Procardia	Anti-anginal
	Seldane	Antihistamine
	Trilisate	Anti-Inflammatory
Subject 5	Catapres	Antihypertensive
	Coumadin	Anticoagulant
	Ferrous Sulfate	Iron Supplement
	Loniten	Antihypertensive Vasodilator
	Lopressor	Beta Blocker
	Nephrocaps	Mineral/Vitamin Supplement
	Os-Cal[b]	Calcium + Vitamin D
	Restoril	Benzodiazapine Sleeping Drug
	Tagamet	Anti-ulcer
	Vibramycin	Tetracycline Antibiotic

Table 4.20 (cont'd)

Subject 6	Cephalexin	Cephalosporin Antibiotic
	Chorzoazone	Muscle Relaxant
	Citracal	Calcium Citrate Supplement
	Ferrous Sulfate	Iron Supplement
	Nephrocaps	Mineral/Vitamin Supplement
	Promethazine	Antihistamine/Anti-emetic
	Propoxy Wygesic	Non-Narcotic Analgesic
	Tylenol[c]	Analgesic
Subject 7	Alu-Caps	Phosphate Binder
	Centrum	Multivitamin Supplement
	Ducolax	Laxative
	Ferrous Sulfate	Iron Supplement
	Sodium Bicarbonate	Antacid
	Tylenol	Analgesic
Subject 8	Citracal	Calcium Citrate Supplement
	Tylenol	Analgesic
	Vitamin B + C	Vitamin Supplement
Subject 9	Alternagel	Phosphate Binder
	Citracal	Calcium Citrate Supplement
	Colace	Laxative
	Nephrocaps	Mineral/Vitamin Supplement
	Nepthazane	Carbonic Anhydrase Inhibitor Diuretic
	Rocaltrol	Vitamin D Supplement
	Tylenol	Analgesic
Subject 10	Allopurinol	Drug for Gout
	Calcium	Calcium Supplement
	Capoten	ACE Inhibitor
	Clonidine	Antihypertensive
	Isoptin	Anti-angina/Anti-arrhythmic
	Minoxdyl	Antihypertensive Vasodilator
	Nephrocaps	Mineral/Vitamin Supplement
	Tabron	Vitamin/Mineral Supplement
	Zyloprim	Drug for Gout
Subject 11	Benadryl	Antihistamine/Anti-emetic
	Catapres	Antihypertensive
	Darvocet	Analgesic
	Keflex	Cephalosporin Antibiotic
	Klonopin	Benzodiazapene Anticonvulsant
	Oyster Shell Calcium	Calcium Supplement
	Restoril	Benzodiazapene Sleeping Drug
	Rocaltrol	Vitamin D Supplement
	Zantac	Anti-ulcer

Table 4.20 (cont'd)

Subject 12	Ascriptin	Antacid/Analgesic
	Ferrous Sulfate	Iron Supplement
	Klonopin	Benzodiazapene Anticonvulsant
	Lasix	Loop Diuretic/Antihypertensive
	Nephrocaps	Mineral/Vitamin Supplement
	Os-Cal	Calcium + Vitamin D
	Phos-Ex	Phosphate Binder
	Prednisone	Corticosteroid
	Quinamm	Anti-malarial
	Tenex	Antihypertensive
	Tums	Antacid
Subject 13	Belladonna	Irritable Bowel Syndrome Drug
	Calcium	Calcium Supplement
	Carafate	Ulcer Healing
	Docusate Sodium	Stool Softener
	Ex-Lax	Stimulant Laxative
	Keflex	Cephalosporin Antibiotic
	Motrin	Nonsteroidal Anti-inflammatory
	Nephrocaps	Mineral/Vitamin Supplement
	Procardia	Anti-angina/Antihypertensive
	Quinamm	Anti-malarial
	Tagamet	Anti-ulcer
	Vicodin	Analgesic
Subject 14	Alu-Caps	Phosphate Binder
	Aspirin	Analgesic/Antiplatlet
	Ferosol	Iron Supplement
	Lanoxin	Digitalis
	Nephrocaps	Mineral/Vitamin Supplement
Subject 15	Bactrim	Sulfonamide Antibacterial
	Benadryl	Antihistamine /Anti-emetic
	Calan SR	Calcium Channel Blocker
	Catapres	Antihypertensive
	Citracal	Calcium Citrate Supplement
	Dilantin	Anticonvulsant
	Ferrous Sulfate	Iron Supplement
	Halcion	Benzodiazapene Sleeping Drug
	Nephrocaps	Mineral/Vitamin Supplement
	"Pain Pill"	Analgesic
	Tenormin	Antihypertensive

[a]Required in Period II, not needed in Period IV, Subject was on fiber supplement during Period IV.
[b]Dosage increased (doubled) during Period IV, Subject was on fiber during Period IV.
[c]Did not take during Period IV, Subject was on fiber during Period IV.

Drugs taken by subjects which have the potential for producing constipation and/or diarrhea are shown in Table 4.21. Of the fifteen subjects in the study, 12 (73%) were on daily doses of a medication that was potentially constipating when taken as recommended (e.g. no overdose or excessive use). Two subjects (7%) were on occasional doses of a medication that was potentially constipating. Seven of the subjects were on occasional doses of a medication which could potentially cause diarrhea. The subjects remained on these medications during the study as they were essential to their treatment as a dialysis patient. Because there were so few differences between periods in dosages required and in most cases only one person was on any particular drug listed in Table 4.21, it is unlikely that drugs directly contributed to the changes in prevention or treatment of constipation observed with fiber supplementation.

Each week subjects responded to the written statement asking if they had noticed "changes in the way their medications affected them" (Table 4.22). During the eight week study, there were seven individual comments on changes in medication. Only one of the comments related to bowel habits; one subject noticed that his/her calcium supplement did not seem to be as constipating. This subject was in group B and noted this change during week four of the study; therefore, while on the fiber cookie. Another subject reported starting on both Catapres and Halcion during week six and seven of the study. This subject reported nightmares in association with the medication. It is unlikely that the medication interacted with the treatment to result in this side effect. The subject was in group B, and therefore on the sugar cookie treatment

during those weeks of the study. In general, with the exception of the subject on the calcium supplement, the reported change in general condition as a result of medications was not significant. Thus, the dosages required (Table 4.20) and self-reports (Table 4.22) suggest that the fiber supplement did not significantly affect the medications taken by the subjects or their efficacy.

Table 4.21 Medications taken by subjects and relationship to constipation and/or diarrhea[a]

Subject (n)	Medication	Class/Type	Const.	Diar.
1	Alternagel	Phosphate Binder	Yes	
4	Alu-Caps	Phosphate Binder	Yes	
1	Ascriptin	Antacid/Analgesic	Yes	
1	Belladonna	Irritable Bowel Syndrome	(R)Yes	
1	Calan SR	Calcium Channel Blocker	Yes	
1	Carafate	Ulcer Healing	Yes	(R)Yes
1	Cardene	Calcium Channel Blocker	Yes	
2	Catapres	Antihypertensive	Yes	
1	Cephalexin	Cephalosporin Antibiotic		Yes
4	Citracal	Calcium Citrate	(E)Yes	
1	Clonidine	Antihypertensive	Yes	
1	Colace	Laxative	(O)Yes	(E)Yes
1	Darvocet	Analgesic	(R)Yes	
1	Docusate Na	Laxative	(O)Yes	
1	Doxycycline	Tetracycline Antibiotic		(R)Yes
1	Ducolax	Laxative		(R)Yes
1	Ex-Lax	Stimulant Laxative		Yes
1	Isoptin	Anti-angina/Antiarrhythmic	Yes	
1	Kayexylate	Cation Exchange Resin	(E)Yes	
2	Keflex	Antibiotic		Yes
1	Motrin	Non-steroidal Inflammatory	Yes	Yes
2	Os-Cal	Calcium + Vitamin D	(E)Yes	
1	Peri-Colace	Stimulant Laxative	(E)Yes	(O)Yes
1	Propoxy Wygesic	Non-Narcotic Analgesic	(R)Yes	
2	Quinamm	Antimalarial		Yes
2	Tagamet	Anti-ulcer		(R)Yes
1	Theophylline	Bronchodilator		(R)Yes
1	Tenex	Antihypertensive	(R)Yes	
1	Vibramycin	Tetracycline Antibiotic		(R)Yes
1	Zantac	Anti-ulcer	(R)Yes	

[a]Information relative to side effects of the drugs was obtained from Physicians' Desk Reference and AMA Guide to Prescription and Over-The-Counter Drugs, n=15.
[b](E) = excessive use, (O) = overdose, (R) = rare occurrence.

Table 4.22 Report of changes in medications by subjects[a]

Noticed changes in how medication affected him/her this week[b]		No Change(n)	(n) Changes noted with Comments
Period I	(week 1)	15	0
Period II	(week 2)	14	1 (Seldane working)
	(week 3)	15	0
	(week 4)	14	1 (calcium not constipating)
Period III	(week 5)	14	1 (Bumex working)
Period IV	(week 6)	13	1 (Bumex working) 1 (Catapres causing nightmares)
	(week 7)	14	1 (Halcion causing nightmares)
	(week 8)	15	0

[a]Data from form F (medication record), and weekly checklist, n=15.
[b]Self-reported on weekly checklist by subjects.

Evaluation of Study by Subjects

Table 4.23 relates information from the study evaluation questionnaire. Of the subjects that completed the study, fourteen (14) returned this questionnaire. Most subjects had some positive comments when asked what they liked best about participating in the study. Subjects reported the research may help other people (5 subjects), there was more contact with the dietitian (2), it helped to stabilize or keep their bowels more regular (2),the cookies were good to eat (1), he/she learned more about the importance of fiber (1), and the study was interesting (1). Two subjects gave no comment to that question.

Comments made about the least liked part of participation ranged from the number of cookies eaten per day (3 subjects), the packaging of the cookies (1), writing food records (1), measuring the foods (1), and

needing to consume the cookies on a daily basis (3). Five of the subjects gave no negative comment to this question.

All fourteen subjects who returned the questionnaire reported that they would be willing to participate in a similar study if one were to be conducted in the future.

Fifty-seven percent (57%) of the subjects returning the questionnaire reported that there had been a change in bowel habits since the end of the study. Comments listed included bowels not moving as well; less bowel movements; stool tightened up; stools harder now; and have now added a high fiber cereal to my diet and am not as constipated as prior to the study.

Table 4.23 Subject evaluation of study[a]

	Positive response (n)[b]	Negative response (n)
Liked best in participation.	Interesting (1) May help others (5) More contact with dietitian (2) Eating cookies (1) Stabilize/keep bowels regular (2) Learned importance of fiber (1) No comment (2)	None
Liked least in participation.	No negative comment (5)	Number of cookies (3) Writing food record (1) Measuring foods (1) Cookies daily (3) Cookie packaging (1)

	Yes % (n)[c]	No % (n)
Change in bowel function since end of study.	57 (8)	43 (6)
Would participate in similar study again.	100 (14)	0 (0)

[a]Self reported data from study evaluation questionnaire, not all subjects returned a questionnaire, all responses were anonymous, n=14.
[b]Responses of subjects (number reporting each response).
[c]Percent of those responding (number of subjects).

CHAPTER V

DISCUSSION

Introduction

The renal hemodialysis patient often suffers from complications that may include constipation, diabetes, Type IV hyperlipidemia, and diverticulosis (Cochran, 1982; Guranieri et al., 1980; Levine, 1982; Zeman, 1983,1990). Some of these complications (such as constipation) may be related to the necessary diet restrictions and medications, as well as the sedentary lifestyle of the hemodialysis patient (Adams, 1982; Burgess, 1987; Chambers, 1983) Fiber supplementation was seen as a possible valuable addition to the diet of the renal hemodialysis patient as inclusion of fiber has been shown to have positive effects in patient populations with such conditions as constipation, diabetes, hyperlipidemias, and some gastrointestinal tract disturbances (Anderson, 1985; 1986; Anderson et al., 1979; 1987; 1990; Astrup, 1989; Cummings, 1978; Jenkins, 1988; Kay, 1982; Simpoulos, 1986).

This study was conducted to determine the possible benefits and disadvantages of addition of insoluble fiber to diet of hemodialysis patients. The eight week cross-over design study was initially begun with 22 subjects selected from a pool of those subjects who met specified criteria as listed in the sample and subject selection section of the methods chapter. Whether subjects suffered from constipation was not a selection criterion because the overall aim of the study was to

evaluate the effects of an insoluble fiber product in hemodialysis patients. Twenty-two was chosen as a reasonable number of subjects considering the length of the study, the involvement, and time commitment of the subjects, and the cost of collection and analysis of the data to be obtained during the study. Four of the subjects withdrew during the first week of the study. Two of the subjects withdrew due to inability to complete all the forms on a daily basis that would be necessary for subject participation. One subject stated that the study would interrupt his normal lifestyle. One other subject perceived that the control cookie had an undesirable side effect of diarrhea. Three additional subjects were excluded from the final data analysis due to failure to meet the criterion of having consumed at least three cookies each day during the treatment period during which they received fiber. Total cookies consumed per day was determined by analyzing data from cookie consumption records kept during the treatment periods. Analysis was completed on all data from the fifteen remaining subjects (68% of starting population).

The Sparrow Hospital Renal Dialysis Unit was an appropriate research site because of the close working relationship between the Renal Dietitian (Diane Fischer, M.S., R.D.) and Dr. Bond (the graduate researcher's major professor), and the support of the staff. The proximity of the unit to Michigan State University was also an advantage. The Sparrow Hospital staff assisted when needed and were very cooperative and helpful throughout the entire study. Overall, conducting this study helped to benefit both the hospital and Michigan State University. When the study was reviewed by the Sparrow Hospital Institutional Research and Review Committee, the group commented that

the project addressed a patient population that had been overlooked in research. The committee also complimented the researchers on establishing this linkage between Sparrow Hospital and Michigan State University.

An insoluble fiber supplement added to a baked product was selected for the study. In this way, a measured amount of fiber could be given and subjects could easily record their intake. The amount of fiber (approximately 14 g) was calculated prior to the study to approximately double typical dietary intake of the subjects. The dietary fiber intake during the baseline periods was 9.93 ± 4.70 grams and 11.40 ± 6.26 grams; therefore, preliminary estimates approached actual values. Fibrad was selected because it has been analyzed to contain 80% dietary fiber by weight, of which 90% is insoluble and comes from insoluble fiber sources other than wheat bran which has been investigated previously by other researchers. The supplement is low in sodium, potassium, and phosphorus, which are of concern in the hemodialysis patient population. Also the supplement was easily incorporated into a palatable baked product.

An eight (8) week study was selected for several reasons. It was determined to be an adequate period of time to observe any change in those factors being studied such as bowel function, while still maintaining the interest of the population being studied (e.g. subject compliance to study protocol). The eight week time period was also chosen to keep costs in a reasonable range.

Hypothesis 1

Fiber supplementation will be effective in treating/preventing constipation in the renal hemodialysis patient.

Constipation is a common symptom reported by hemodialysis patients, and may be related to diet restriction of high potassium foods (including many fruits and vegetables) and high phosphorus foods (including whole grain products); fluid restriction; medications (including aluminum antacids used as phosphate binders); and sedentary lifestyle (Adams, 1982; Burgess, 1987; Chambers, 1983; Ghose, 1970; Welch, 1980). The word constipation does not have one all encompassing definition. Most definitions do include infrequent bowel action (fewer than three per week) and defecation of hard stools; and also may refer to sensation of pain on defecation , reduction in frequency of defecation, and incomplete evacuation of feces (Harrison, 1983; Ross Laboratories, 1990; Sandler, 1990; Taylor, 1990; Zeman, 1983).

Data collected from subjects at the initiation of the study, and presented in Tables 4.4, 4.5, and 4.6 show that constipation was a problem for some of the subjects in the study.

Results from information gathered during the study did not show a tremendous difference between the treatment periods and the baseline periods for average number of stools and stool consistency. Reported values for stool consistency and average number of stools did not show a statistically significant difference between periods or treatments (Table 4.11). However, the daily general condition questionnaire used alone may not have been sensitive enough to detect subtle changes in

individual subject bowel function. A collection and measurement of stools would have given a definite measure of changes in weight and consistency. It was not, however, a reasonable measurement to obtain in this study, as this was an outpatient population, and the study was structured for minimal interference with the subjects' normal daily schedules over 57 days.

The daily report of constipation (Table 4.10) does show a trend when examining the percentage of those reporting constipation over the course of the study. The trend reveals that group A reported an increase in reported constipation (17%) from the baseline period to the control treatment, and a subsequent decrease in reported constipation (48%) from baseline to the fiber treatment. Group B reported a 48% decrease in constipation from the baseline to the fiber treatment, and a subsequent 29% increase from the baseline to the control cookie treatment. There was no effect of treatment found with pain on defecation.

Subjects reported at the end of the treatment period on the general effects of the cookie. Of the fifteen subjects, nine (60%) reported that the fiber cookie made their bowel movements more regular , compared to seven (47%) with the control cookie. Nine subjects (60%) also reported that the fiber cookie made their bowel movements more comfortable, as compared to eight subjects (53%) with the control cookie (Table 4.13). The possibility of a placebo effect cannot be ignored.

In completing the study evaluation questionnaire three months after the study, 57% (n=8) of subjects stated they had noticed a change in bowel function since the study ended (Table 4.23). Comments listed included: " bowels not moving as well; less bowel movements; stool

tightened up; stools harder now; and have now added a high fiber cereal to my diet and am not as constipated as prior to the study."

During a phone interview six months after the study had taken place the subjects were asked two questions. The first question asked was "Could you tell which time you had the fiber cookies -- was it the first or second time you were on the cookies?" The second question asked " What was the difference you noticed between the two periods?" Of the twelve subjects which could be contacted, 66.7% (n=8) were able to correctly identify when they were on the fiber cookie treatment (Table 4.14). Most of the differences noted by the subjects who correctly identified the fiber cookie treatment were related to bowel function and included such comments as: " made my bowel movements softer; made stools easier to pass; made bowel movements more regular; gave a looser stool that was easier to defecate. "

These results show that although there was no statistical difference found between the treatments on stool number or consistency, the subjects reported a 48% decrease in constipation from baseline when on the fiber supplement cookie, and 60% of subjects reported that the fiber cookie made their bowel movements both more regular and more comfortable as compared to the baseline period. Because of the sample size, statistical analysis was limited. However, it does appear that over half of the subjects perceived the fiber cookie as helping to normalize their bowel habits. This evidence is especially striking in view of the fact that all subjects did not initially report suffering from constipation, and would not have been expected to benefit from the fiber supplement. In summary, there is evidence that the addition of

the insoluble fiber to the diet aided in control and prevention of constipation in this subject group.

Hypothesis 2

Fiber supplementation will not increase gastrointestinal symptoms (cramping, bloating, gas, diarrhea, etc.) of the renal hemodialysis patient.

The addition of fiber to the diet may cause temporary unpleasant gastrointestinal side effects such as nausea, cramping, bloating, and gas (Anderson, 1986; AMA Council on Scientific Affairs, 1989; Taylor, 1990). This could affect the compliance of an individual to a regimen that included a fiber supplement. Measurements reported associated with gastrointestinal side effects included nausea, abdominal cramping, diarrhea, gas, and intestinal rumbling.

Nausea was not reported to be a problem for most subjects on either treatment as can be seen in Table 4.12. Group B appeared to be somewhat affected in reported abdominal cramping in both treatment periods, whereas group A did not seem to be affected by either treatment. There was a small percentage increase in intestinal rumbling (from baseline) for both treatments in both groups. There was not a consistent change for either group for the treatment periods in the intestinal gas category. Thus, there appeared to be no consistent changes in gastrointestinal symptoms with fiber treatment when compared to baseline or control sugar cookie treatment.

There was no clear increase/decrease relationship for the fiber treatment when looking at the reported diarrhea during the treatment periods (Table 4.10). The fiber cookie appeared to decrease the diarrhea in group B (n=9) and increase the diarrhea in group A (n=6).

Hypothesis 3

Fiber supplementation will not reduce food intake of the renal hemodialysis patient.

The definition of food intake for this study was viewed as total calories consumed (energy). The hypothesis would then be taken to mean that the subjects would not consume a significantly fewer number of calories per day during the fiber supplement treatment period as compared to the control treatment period or baseline periods.

The use of a food record was chosen based on the need for collection of data on actual portions of food consumed. This method has been studied and determined to give a reasonably accurate measurement of actual food consumed (Block, 1982). The selection of three days was based on consideration of the population of subjects being studied, and on data presented by Chalmers et al. (1952) on precision derived when increases in number of days of keeping a diet record were performed.

The selection of the use of the Minnesota Nutrient Data System version 2.2 as the program for analysis of the food and beverage records was based on several factors. A literature search of currently available nutrient data bases was conducted, as well as consultation with those at Michigan State University who have expertise in the area

of nutrient data bases. Several nutrient data bases were given a trial run using six of the diet records. Selection was then made based on completeness of data base, ease of use, and currentness of the data base. The Minnesota Nutrient Data base has over 16,000 foods, and was more complete than other data bases reviewed in nutrients (such as dietary fiber) that were of interest to this study (Feskanich, 1989; Mitchell, 1991; NCC, 1990). Only three (3) of the foods listed on the diet records were not immediately available in the data base.

Studies with obese populations have reported that addition of fiber to a controlled diet significantly decreased hunger ratings (Astrup et al., 1989), and increased satiety (Anderson, 1986). It was deemed necessary to determine if addition of the fiber supplement cookie would decrease food intake of the subjects. Maintenance of nutritional status is important in the hemodialysis population; therefore, a decrease in food intake or total energy (kilocalories) consumed would not be considered beneficial.

Subjects consumed significantly more kilocalories in the control and fiber periods than in the baseline (Table 4.18). Therefore, the addition of the fiber supplement did not decrease the food intake. The cookies contributed approximately 461 kilocalories per day. It is interesting to note that the subjects' weights were not different throughout the study (Table 4.6). The discrepancy in total calories may have been due to under-reporting on the diet records in the baseline periods, or the adjustment of intake during the treatment periods by the subjects that was not reflected in the three day diet records.

Hypothesis 4

Fiber supplementation will not affect the fasting blood concentrations of potassium, phosphorus, calcium, cholesterol, triglycerides, high density lipoproteins, creatinine, urea, glucose, iron, or ferritin in the renal hemodialysis patient.

It is important for the treatment and medical status of the hemodialysis patient, that certain serum blood values remain within a specified range. Because the kidney is no longer functioning, it is important to control the waste products that now must be taken out of the body through hemodialysis treatments. This control is done in a large part through dietary restriction and medications (Zeman, 1990). Because supplementation with fiber may alter the diet of the hemodialysis patient, and previous research has shown some fibers can influence concentration of blood constituents (Anderson, 1985; Anderson et al., 1987; 1990; deGroot et al., 1963; Hagander et al., 1989; Hamberg et al., 1989; Jenkins et al., 1975; Parillo et al., 1988) , fasting blood samples from subjects during each of the periods the research study were analyzed. Results are reported in Table 4.17. Of the blood constituents tested, there was no statistically significant difference in the concentration of blood urea nitrogen, creatinine, phosphorus, glucose, cholesterol. triglycerides, HDL, cholesterol, iron, or ferritin during baseline and treatment periods. There was a statistically significant difference found between the two treatments given for serum potassium ($p=0.015$) and calcium ($p=0.017$). This direct treatment effect found that the control (sugar cookie) treatment resulted in

significantly higher serum values for both potassium, and calcium. While the difference was considered to be statistically significant, it should be mentioned that all serum values for potassium and calcium remained in what is considered a physiologically normal range as per reference ranges used by LifeChem Laboratories (Table 4.17) and generally acceptable in the clinical laboratory (Pagana and Pagana, 1990). The results of this study cannot surmise the long term effect of fiber supplementation on serum calcium values, or whether this decrease would become of physiological importance with extended use.

Hypothesis 5

Fiber supplementation in the form of a fiber cookie will be an acceptable (palatable) way to incorporate fiber into the diet of the renal hemodialysis patient.

Incorporation of fiber into the diet of any population can be a challenging task. Researchers have used various methods of incorporation of fiber into the diet of subject populations including the use of oat bran muffins (Anderson et al., 1984), dry beans (Anderson et al., 1984), fiber sources incorporated into bread (deGroot et al., 1963; Hagander et al., 1988; Wrick et al., 1983), and coarse wheat bran (Burgess, 1987). Although the intentions of increasing fiber may be very well meant, if the method of incorporation is not acceptable to the population, there will be no long term commitment to continue its use (Hoover, 1989; Taylor, 1990). It was, therefore, important to develop a product that would be acceptable to the test population. The fiber

cookie itself had been developed at Michigan State University, and pilot tested with faculty and graduate students, as well as staff and patients at Sparrow Hospital. However, it was also important to obtain feedback from the subjects who had been consuming approximately four cookies per day for the three week treatment period, to assess the acceptability of the product as a possible continued part of the diet. Table 4.8 has the scores received by both the control and fiber cookies at the conclusion of the treatment periods. There was no statistically significant difference found between the control sugar cookie and the fiber supplement cookie on the characteristics of flavor, texture, taste, aftertaste, ease to chew and swallow, ability to tolerate every day, and overall evaluation. The mean scores ranged between 4 (neither like nor dislike) and 6 (like slightly) for both cookies. This is viewed as a positive outcome for the fiber cookie. It ranked as well as the control sugar cookie, and was accepted by the subject population. If there had been any change in acceptability of the fiber supplement cookie over the course of the treatment period, it may have resulted in decreased consumption of cookies during that treatment period, and therefore jeopardized the outcome of the study due to inadequate intake of fiber by standards defined in this study (e.g. < three cookies or < 10.5 grams additional dietary fiber).

An advantage of the fiber source used in this study is that it is in a powder form and could be easily incorporated into other food products. In the future subjects may be able to use this supplement in foods and beverages that they consume on a regular basis without greatly altering the acceptability.

Hypothesis 1 (secondary)

Fiber supplementation will not affect the dry weights or between dialysis weight (interdialytic) gains in the renal hemodialysis patient.

The hemodialysis patient is very often restricted in the amount of liquid he/she is allowed to consume each day. Fluid is restricted due to the inability of the kidney to filter the excess fluid that is not needed by the body (Burton et al., 1983; Chambers, 1983; Zeman, 1983; 1990). It was important in this study to look at the effect that the fiber supplementation might have had on the fluid status of the individual. Data gathered from the medical charts of the subjects during the study included the pre and post-dialysis weights. From these data the average weight gain for each period and the average interdialytic weight gain for each period was calculated for each subject. Weight data are shown in Table 4.16 for each group during each period of the study. When the treatment by period interactions were taken into account, there were no statistically significant treatment effects found. Other factors taken into consideration were the time on dialysis, need for transfusion, and administration of saline during dialysis sessions. There were no differences found over the course of the study for subjects in relation to these three variables.

The amount of fluid ingested by the subjects was also recorded on the diet records that were collected for three days of one week of each of the study periods. The records were analyzed by the Minnesota Nutrient Data System (version 2.2) for water content in grams. The total amount of water in the food and beverages consumed was averaged

for three days of each period for each subject (Table 4.18). This set of three day averages was analyzed using a paired t-test. No statistical difference in fluid intake was noted for any of the periods.

The interpretation of these data would suggest that the fiber cookie did not affect the overall fluid retention, or dry weights of the subjects in the study. The fiber cookie did not absorb enough extra fluid from that which was ingested in the diet to show a statistical difference in interdialytic weight gains during the period in which subjects were on the fiber treatment. Based on these results the addition of the fiber cookie to the diet of the hemodialysis patient would not automatically merit an increase in the daily amount of fluid presently allowed, but also would not require additional restriction of fluids.

Hypothesis 2 (secondary)

Fiber supplementation will not affect the diet or medication compliance of the renal hemodialysis patient.

Analysis of the diet records showed no statistical difference in the amount of protein, potassium, phosphorus, sodium, cholesterol, and water ingested during the baseline, and control and fiber periods. There were statistical differences between the baseline periods and both treatments (though no difference between the treatments themselves) for energy, total fat, and total carbohydrate. The differences in these cases may have been associated with the ingestion of the cookies during the treatment periods without a decrease in the other foods consumed.

The ingestion of the average number of cookies eaten (3.66) would have introduced approximately an extra 461 calories, 55 grams of carbohydrate, and 25-26 grams of fat per subject per day. It should be mentioned that although the energy is significantly different, the average dry weights of the subjects did not increase over the course of the treatment periods as one would expect if the extra calories were ingested on a daily basis. This may point to a possible under reporting of foods consumed during the baseline periods, or a compensation effect during those days when the subjects were not recording their dietary intake.

There was also a significant difference found in the amount of dietary fiber and insoluble fiber ingested, with the fiber treatment being significantly higher than the control and baseline periods. This would seem to follow in a logical fashion considering that each fiber cookie contained approximately 3.63 grams of dietary fiber, and the differences in the dietary fiber amounts in Table 4.18 appear to be accounted for by subtracting out the amount of fiber the cookies would have contained. There were also significant differences in the amount of calcium ingested during the fiber treatment period as compared to the control period and in the amount of iron ingested during the control period as compared to the baseline periods. These results are interesting, but not easily accounted for by the treatments that were given, and may have had to do with individual differences in dietary consumption patterns.

Diet record data were analyzed using paired t-tests. Data were not analyzed using a multiple omnibus test. It should be noted that although t-tests were an acceptable way to analyze these data, the

number of t-tests run may have slightly increased the possibility of a type I error at the $p \leq 0.05$ level.

The three day average nutrient intakes diet records were compared to the diet prescriptions as taken from medical charts and the background information form (Form A) to check on deviation from compliance in relation to the study for potassium, sodium, protein, phosphorus, and fluid. As can be seen from Table 4.16 only one (7%) of the fifteen subjects was not compliant during only the treatment periods on the protein restriction part of the diet. Five subjects were noncompliant during both a treatment period and a baseline period (one subject (7%) with protein, and two subjects (13%) each with sodium and potassium). Four additional subjects (27%) were noncompliant to the protein restriction during all periods of the study. Also, three subjects (20%) were noncompliant to the sodium restriction during all four periods. This reveals that in the case of the subject noncompliant only during the two treatment periods, there may be a noncompliance association exclusive to the treatments given. Overall, the treatments did not interfere with the subjects' compliance with diet restrictions or fluid restrictions.

Table 4.20 lists all the medications that the subjects were on during the research study, as reported on Form F. Dosages of medications were not affected by the treatments in most cases. In the three subjects where the dosages do vary, it seems unlikely that the treatments caused a change in the subject who had fluctuations in use of Os-Cal, and the subject who had fluctuations in the use of Tylenol.

The subject who had a decrease in use of Peri-Colace during the fiber treatment period as compared to the baseline and sugar cookie treatment period may have had an effect due to the treatment itself.

The results from the weekly comments and medication records as reported in Table 4.22 reveal that there were several changes noted in how medications affected the subjects, but only one reference to the treatment itself. One subject mentioned during week four (which was the fiber treatment for this subject), that the calcium supplement normally taken was not as constipating as it had been. It can be concluded that with the exception of the subject that decreased the use of Peri-Colace, neither treatment seemed to cause noncompliance to the medications normally consumed. However, the reports of how medications affected the subjects is a limiting factor in the study because the changes noted were self-reported.

CHAPTER VI

LIMITATIONS, STRENGTHS, CONCLUSIONS AND RECOMMENDATIONS

Assumptions

It was assumed that all subjects answered all questions honestly, and followed the investigation procedures as instructed. It was assumed that the subjects consumed the fiber or control sugar cookies as directed, and that they reported food consumption accurately. It was also assumed that the blood specimens were handled and analyzed properly. It was assumed that all dietary record data were entered correctly and that the diet analysis data base was as complete as currently available, especially with respect to fiber and constituents of special interest in this study.

Limitations

There were some limitations to this study. The use of human subjects gives the possibility of error, as humans vary biochemically and physiologically, and are motivated (or deterred) by many different environmental and personal factors. This study was conducted using a human population as the questions it poses relate directly to specific common complication(s) of the End Stage Renal Patient on hemodialysis. It was not logical to apply this research to an animal population, as

this would not have helped to answer any of the proposed hypotheses. The research design, instruction of the subjects, checking of forms for completeness, and personal encouragement of all study subjects attempted to minimize this limitation. Also the amount of fiber (14 grams) that was added, was a limitation. This study does not show the effect of higher amounts of fiber in this population. Although this amount doubled the normal intake of the hemodialysis patient, some studies with other fibers have used two or more times this amount. Another limitation was the preparation of the cookies. It had to be assumed that the cookies, if prepared by a standardized recipe, would yield a product that was of the approximate composition of the ones made when standardizing the recipe. The cookies made in mass quantities may have varied somewhat depending on the thoroughness of mixing. The use of institutional mixing equipment, an experienced baker and, a common lot of ingredients helped to somewhat compensate for any possible differences.

Another limitation was that subjects could not be removed from medications during the study. This subject population was unique in the variety and doses of medications that they were taking on a daily basis. Even though most of the subjects took the potentially constipating or potentially diarrheal-inducing medications on a daily basis, the changes noted were from self-reports, and the incidence of constipation and diarrhea with the medications involved varies from individual to individual. Because the concentration of drugs was not measured in the body directly, the evidence that fiber supplementation did not affect efficacy is based solely on medication records and subjects' responses related to side effects.

Other limitations include the length of the study, and the specificity of the population. This was a relatively short term study and did not provide information on the long term effects of supplementation with the product being used. The results of this study are generalizable to a universe similar to the one in which the subjects were obtained. Chronic hemodialysis patients age 34 to 77 taken from a population at a hospital in central Michigan do not necessarily characterize all hemodialysis patients nation wide. Also, the use of this specific clinical population somewhat compromises the external validity of the study. The randomization of the assignment to treatment groups helped to control for this limitation.

Strengths

The specificity of the population studied was also a strength of the study. Because the population studied was so specialized, the results of the study are directly applicable to that population of hemodialysis patients.

Another strength of the study was the length of the study. An eight week study using an outpatient population that requires the subject to keep daily records and consume four cookies per day for six out of the eight weeks that finishes with a large percentage of its initial population is a respectable accomplishment. This study also includes a group of subjects with a large age range and a variety of medical conditions. There was great attention given to the diet, medications, and general condition of the subjects. This study also reaped a wealth of dietary information that is one of the most

comprehensive evaluations available of what renal (hemodialysis) patients are eating. An extensive data base of dietary intake on these subjects is available for further analysis of research questions beyond the hypotheses addressed in this thesis.

Conclusions

There are several conclusions that can be drawn from this research study. First, fiber supplementation using insoluble fiber from a product that contains oat, pea and sugar beet fibers at the level used (approximately 14 grams) normalized bowel function for at least half of the subjects. This was evidenced by self-reports of a decrease in reported constipation from baseline with the fiber treatment, from the response of changing bowel function on the evaluation of fiber research study form, and the answers on the six month post-study follow-up phone interview during which 66.7% of the subjects correctly identified the fiber treatment period making reference to softer , more frequent, and/or more easily passed stools. The fiber supplementation also did not appear to cause any consistent adverse gastrointestinal effects (e.g. cramping, nausea, intestinal rumbling, intestinal gas).

Fiber supplementation did not appear to adversely affect the serum blood values for blood urea nitrogen, creatinine, phosphorus, potassium, glucose, cholesterol, triglycerides, iron, high density lipoprotein, or ferritin. Iron values remained well within the normal range; however, most of the subjects were on iron supplementation as anemia is a condition often found in hemodialysis patients. The fiber treatment did appear to decrease serum calcium, but, the serum calcium remained in

what is considered a normal physiological range. It should be noted that this was a short term study; it is not known what effects the fiber supplementation would have on blood constituents over a longer period of time.

The product used for fiber supplementation was an acceptable one to be incorporated into the diet, as can be concluded from the scores the cookie with fiber received on the cookie evaluation. Fiber supplementation did not reduce the food intake of the subjects as seen by the total number of energy (calories) consumed. The fiber supplementation significantly increased the intake of total fat, total carbohydrate, energy (calories), dietary fiber, and insoluble fiber as compared to the baseline periods. The fiber treatment also significantly differed from the control treatment in amount of dietary fiber, insoluble fiber, and calcium. Fiber supplementation did not appear to affect compliance to diet prescription for most of the subjects in the study.

Fiber supplementation did not have an effect on the dry weight or interdialytic weight of the subjects. It did not, in most cases, appear to affect the compliance of the subjects to their normal medication regimen .

The fiber source used in this research (75% pea, 15% oat, 10% sugar beet) is fairly unique in research of this kind. Research studies have used mainly wheat as the source of insoluble fiber supplementation, which for this population is not feasible due to the high phosphorus and potassium content of wheat fiber. This type of fiber supplementation may work well with other similar populations.

A final conclusion is that the study had a positive effect on the subjects. They were very cooperative throughout the entire study and all commented on the evaluation of study form that they would be willing to participate in a similar type of study again. In addition, five of the subjects commented that the best part about participating in the study was that their participation may help others.

Recommendations For Further Research

This appeared to be the first study using insoluble fiber with an outpatient hemodialysis population. The knowledge gained through conducting the study has application for future research. In future studies, it may be beneficial to use constipation as a screening tool. This study did not screen for constipation, yet found that there appeared to be normalization of bowel function in over half of the subjects while on the fiber treatment when 53% reported having bowel irregularity and only 33% of the subjects reported having problems with constipation at the initiation of the study. If the target population were constipated hemodialysis patients, there may be a greater response rate to the treatment. However, several renal dialysis units may be needed to get the subjects required for such a study.

It may also be of benefit to conduct this type of study over a longer period of time, in which case it may also be interesting to incorporate the fiber in a tablet form. This would give less volume associated with the treatment, a treatment that is more easily stored, the ability to incorporate a larger dose of fiber into the diet, and the ability to maintain or increase acceptance over a long period of time.

This type of a study would need to incorporate a fiber and placebo tablet in the same type of cross-over design.

Although most study subjects reported no alteration in normal medication dosages, it not possible from the data gathered in this study to determine what the effect of the fiber supplement might have been on absorption of drugs and subsequent blood levels of the medications taken. A possibility for future research might include determination of the serum levels of a prototype drug when subjects are supplemented with a pre-determined amount of fiber.

APPENDICES

Appendix 1

Approval from Michigan State University Committee
on Research Involving Human Subjects (UCRIHS)
and Consent Form

MICHIGAN STATE UNIVERSITY

OFFICE OF VICE PRESIDENT FOR RESEARCH
AND DEAN OF THE GRADUATE SCHOOL

EAST LANSING • MICHIGAN • 48824-1046

October 26, 1990

Marci L. Askegard, R.D.
Food Science and Human Nutrition
236 Food Science

RE: THE EFFECT OF FIBER SUPPLEMENTATION IN HEMODIALYSIS,
IRB# 90-379

Dear Marci Askegard:

UCRIHS' review of the above referenced project has now been completed. I am pleased to advise you that since reviewer comments have been satisfactorily addressed, the conditional approval given by the Committee at its October 1 meeting has now been changed to full approval.

You are reminded that UCRIHS approval is valid for one calendar year. If you plan to continue this project beyond one year, please make provisions for obtaining appropriate UCRIHS approval one month prior to October 26, 1991.

Any changes in procedures involving human subjects must be reviewed by the UCRIHS prior to initiation of the change. UCRIHS must also be notified promptly of any problems (unexpected side effects, complaints, etc.) involving human subjects during the course of the work.

Thank you for bringing this project to our attention. If we can be of any future help, please do not hesitate to let us know.

Sincerely,

David E. Wright, Ph.D.
Chairman
University Committee on Research
Involving Human Subjects

DEW/deo

cc: Diane Fischer
Dr. Jenny T. Bond

MICHIGAN STATE UNIVERSITY

DEPARTMENT OF FOOD SCIENCE AND HUMAN NUTRITION

EAST LANSING • MICHIGAN • 48824-1224

Consent Form

I, _____, voluntarily agree to participate in the study conducted by Dr. Raphael Javier, Diane Fischer and staff in the Sparrow Renal Dialysis Unit and Dr. Jenny Bond and Marci Askegard of Michigan State University. I understand that I have been invited to participate because I am on hemodialysis and that the purpose of this research is to determine (1) if a fiber supplement is effective in treating or preventing constipation, (2) what effects, if any, this supplement may have in a person on dialysis, (3) how the supplement may affect blood constituents and (4) if the fiber supplement influences diet or fluid restrictions. I will receive cookies which contain the fiber supplement or regular ingredients as part of my regular care and my treatment will not be affected by my participation in the study. I know that the study will run for 57 days. I know I will be asked some questions about my medical history and response to the cookies. I will be required to keep a record of everything I eat and drink for twelve (12) days during the study period. I know that I will be required to fast overnight for four (4) blood samples of approximately 1 tablespoon to be taken for laboratory examination. I also understand that I will have to provide my social security number in order to receive payment for my participation in the study.

The small risks associated with taking the blood sample have been explained to me. Side effects of taking the fiber supplement have also been explained.

I understand that I may withdraw from this study at any time and it will not affect my care and treatment in the renal unit. I understand that there are no guaranteed benefits to me as an individual from my participation in this program except that I will receive a $ 100 enrollment payment and a $ 100 completion payment. I have had all my questions about this study answered. I understand that all information gathered in this study from me or tests of my blood will be kept in strict confidence (except for sharing with my doctor). All reports of the study will use group results so that individuals will not be identified.

A summary of the results will be provided to me at my request. I understand that if I am injured as a result of my participation in this research project, Sparrow Hospital will provide emergency medical care if necessary. I further understand that if the injury is not caused by the negligence of Sparrow Hospital or MSU I am personally responsible for the expense of this emergency care and any other medical expenses incurred as a result of this injury.

I understand that if I have questions or concerns about my participation in the study, I can contact one of the following:

Diane Fischer - Sparrow Renal Dialysis Unit - Phone: 483-2912
Marci Askegard - Sparrow Renal Dialysis Unit - Phone: 393-0946

Dr. Javier - Sparrow Renal Dialysis Unit - Phone: 483-2843
Betty Whipple - Sparrow Renal Dialysis Unit - Phone: 483-2834
Dr. Jenny Bond - Michigan State University - Phone: 355-1756 or 353-9626

_____ Subject

_____ Researcher

_____ Dr. Javier

_____ Date

I acknowledge receipt of a copy of this consent form.

_____ Subject/Date

Appendix 2

Daily Schedule for Subjects

Daily Schedule for Subjects

Day of Study	Subject's Schedule
Period I	
1	Complete Form A (Background Form). Complete Form F (Medication Form).
2	Complete Form F.
3-7	Complete Form B (General Condition Form). Complete Form F. Complete Form E (Food and Liquid Intake Record) for three nonconsecutive days.
7	Fast from 12p.m. until blood sample is taken on day 8 (day 1 of Period II).
Period II	
8	Have fasting blood sample taken. Consume assigned treatment. Complete Forms B, and F. Complete Form G (Cookie Consumption Record).
9-28	Consume assigned treatment each day. Complete Forms B, F, and G daily. Subjects will complete Form E for three nonconsecutive days during this period.
28	Consume assigned treatment. Complete Forms B,F, and G. Complete Form C (Product Acceptance Form) and D (Product Evaluation Form). Fast from 12 p.m. until blood sample is taken on day 1 of Period III.
Period III	
29	Have fasting blood sample drawn. Complete Forms B and F.
30-35	Complete Forms B and F daily. Complete Form E for three nonconsecutive days of this period.

35	Fast from 12 p.m. until blood sample is drawn on day 36 (day 1 of Period IV).
Period IV	
36	Have fasting blood sample drawn. Consume assigned treatment. Complete Forms B, F, and G.
37-55	Consume assigned treatment each day. Complete Forms B, F, and G daily. Complete Form E for three nonconsecutive days during this period.
56	Consume assigned treatment. Complete Forms B,C, D, F, and G. Fast from 12 p.m. till blood sample is taken on day 57 (day 1 of period V).
Summary	
57	Have fasting blood sample drawn. Complete form that evaluates participation in the study.

Appendix 3

Form A = Background Information

Sparrow-MSU Dialysis Study-1990

BACKGROUND INFORMATION

This form is to be completed by the subject at the beginning of the study (Period I).

Subject Number: _____ Birthdate: _____ Sex: M F

Circle the number below which indicates the correct answer.

1. I have heard about the need for fiber in my diet. 1 Yes 2 No

2. I am concerned about getting more fiber in my diet. 1 Yes 2 No

3. I am bothered by bowel irregularity. 1 Yes 2 No

4. I have been told by a doctor that I have diverticulosis. 1 Yes 2 No

5. I have been told by a doctor that I have hemorrhoids. 1 Yes 2 No

6. Average number of bowel movements per week. _____

7. Stool consistency 0 Loose 1 Soft 2 Firm 3 Hard

8. I am getting increasingly constipated. 1 Yes 2 No

9. I am able to walk freely. 1 Yes 2 No
   If YES, how many hours per day? _____

10. I am able to walk with assistance. 1 Yes 2 No
    If YES, how many hours per day? _____

11. Are you involved in any other types of exercise, besides walking, on a regular basis? 1 Yes 2 No
    If YES, what type? _____

12. Are you taking any stool softeners at the present time? 1 Yes 2 No
    If YES, what brand name? _____
    How much per day do you usually take? _____

13. Are you taking any laxatives at the present time? 1 Yes 2 No
    If YES, what brand name? _____
    How much and how often do you take these? _____

Sparrow-MSU Dialysis Study-1990

14. During the last year I took laxatives for constipation on the average:

    0 Never
    1 Infrequently (no more than 6 times)
    2 Once per month
    3 Once per week
    4 More than once per week

15. During the last year I had diarrhea on the average:

    0 Never
    1 Infrequently (no more than 6 times)
    2 Once per month
    3 Once per week
    4 More than once per week

16. Has the doctor and/or dietitian told you that the potassium in your diet should be limited? 1 Yes 2 No

17. Has the doctor and/or dietitian told you that the sodium in your diet should be limited? 1 Yes 2 No

18. Does your diet contain a fluid restriction? 1 Yes 2 No
    If YES, how much are you allowed per day? _____

19. Does your diet contain a protein restriction? 1 Yes 2 No

20. Does your diet contain a phosphorus restriction? 1 Yes 2 No

21. Medical Diagnoses _____
    _____

Informed consent obtained prior to study enrollment? ___ Yes ___ No

Investigator's Signature _____ Date _____

Appendix 4

Form B = General Condition Form

Sparrow-MSU Dialysis Study-1990

Daily Report of General Condition

This form is to be completed by the subject each day of the study.

Subject Number: _____ Birthdate: _____ Sex: M F

RECORD DAY					
Number of stools each day (Enter 0 if none)					
STOOL CONSISTENCY Circle one most often observed each day	1 Watery, unformed 2 Loose, gassy 3 Softer than normal 4 Normal 5 Firmer than normal 6 Pasty 7 Hard	1 Watery, unformed 2 Loose, gassy 3 Softer than normal 4 Normal 5 Firmer than normal 6 Pasty 7 Hard	1 Watery, unformed 2 Loose, gassy 3 Soften than normal 4 Normal 5 Firmer than normal 6 Pasty 7 Hard	1 Watery, unformed 2 Loose, gassy 3 Softer than normal 4 Normal 5 Firmer than normal 6 Pasty 7 Hard	1 Watery, unformed 2 Loose, gassy 3 Softer than normal 4 Normal 5 Firmer than normal 6 Pasty 7 Hard
CONSTIPATION	0 No 1 Yes	0 No 1 Yes	0 No 1 Yes	0 No 1 Yes	0 No 1 Yes
DIARRHEA	0 No 1 Yes	0 No 1 Yes	0 No 1 Yes	0 No 1 Yes	0 No 1 Yes
HEMORRHOID ATTACK	0 None 1 Itching & burning 2 Required medication	0 None 1 Itching & burning 2 Required medication	0 None 1 Itching & burning 2 Required medication	0 None 1 Itching & burning 2 Required medication	0 None 1 Itching & burning 2 Required medication
NAUSEA	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe
ABDOMINAL CRAMPS or GRIPPING Abdom Cramps of	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe
INTESTINAL RUMBLING	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive
INTESTINAL GAS (Flatus)	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive
Defecation	0 No pain 1 Some pain 2 Much pain	0 No pain 1 Some pain 2 Much pain	0 No pain 1 Some pain 2 Much pain	0 No pain 1 Some pain 2 Much pain	0 No pain 1 Some pain 2 Much pain

Sparrow-MSU Dialysis Study-1990

RECORD DAY		
Number of stools each day (Enter 0 if none)		
STOOL CONSISTENCY Circle one most often observed each day	1 Watery, unformed 2 Loose, gassy 3 Softer than normal 4 Normal 5 Firmer than normal 6 Pasty 7 Hard	1 Watery, unformed 2 Loose, gassy 3 Softer than normal 4 Normal 5 Firmer than normal 6 Pasty 7 Hard
CONSTIPATION	0 No 1 Yes	0 No 1 Yes
DIARRHEA	0 No 1 Yes	0 No 1 Yes
HEMORRHOID ATTACK	0 None 1 Itching & burning 2 Required medication	0 None 1 Itching & burning 2 Required medication
NAUSEA	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe
ABDOMINAL CRAMPS or GRIPPING	0 None 1 Mild 2 Moderate 3 Sustained & Severe	0 None 1 Mild 2 Moderate 3 Sustained & Severe
INTESTINAL RUMBLING	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive
INTESTINAL GAS (Flatus)	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive	0 None 1 Occasional but no more than usual 2 More than usual 3 Excessive
Defecation	0 No pain 1 Some pain 2 Much pain	0 No pain 1 Some pain 2 Much pain

Sparrow-MSU Dialysis Study-1990

DAILY REPORT OF GENERAL CONDITION FORM

Comments: (Complete as necessary)

- -

This week

I FELT	1 Good	2 Fair	3 Poor
I HAD	0 No colds or illness	1 A cold	2 Other medical problems: (list below)

Appendix 5

Form C = Cookie Acceptance Form

Sparrow-MSU Dialysis

Study-1990

COOKIE ACCEPTANCE RECORD - Period II and Period IV

This form is to be completed by the subject at the end of period II.

Subject Number _____

Date _____

1. The cookie did not affect my appetite.	1 Yes	2 No
2. The cookie improved my appetite.	1 Yes	2 No
3. The cookie made my bowel movement more regular.	1 Yes	2 No
4. The cookie made by bowel movement more comfortable.	1 Yes	2 No
5. The cookie is convenient to take any time of the day.	1 Yes	2 No
6. The cookie decreased my appetite.	1 Yes	2 No
7. The cookie filled me up.	1 Yes	2 No
8. The cookie left me hungry.	1 Yes	2 No
9. The cookie is as effective as other laxatives I have used.	1 Yes	2 No
10. The cookie is more effective than other laxatives I have used.	1 Yes	2 No
11. The cookie is more convenient than other laxatives I have used.	1 Yes	2 No
12. The cookie made my bowel movements less regular.	1 Yes	2 No

Comments:

Appendix 6

Form D = Cookie Evaluation Form

Sparrow-MSU Dialysis Study-1990

COOKIE EVALUATION RECORD - Period II and IV

Subject Number _____

Date _____

Please use the 7 point scale listed below for evaluation:

How did you like the cookies this week?

7 I like it very much

6 I like it moderately

5 I like it slightly

4 I neither like nor dislike it

3 I dislike it slightly

2 I dislike it moderately

1 I dislike it very much

A. Flavor _____

B. Texture _____

C. Taste _____

D. Aftertaste _____

E. Easy to chew and swallow _____

F. Can tolerate and take very day _____

G. Overall evaluation _____

Comments:

Appendix 7

Form E = Complete Daily Food and Liquid Record

Subject Number _____

Record for what day _____

Completeness checked by _____

Sparrow - MSU

Dialysis Study

1990

Daily Record of Consumption of Food and Beverages

BEFORE YOU START

Read the following instructions and study the examples.

Record all food, supplements, and other items consumed (for example, water, coffee, beer) on the days specified.

FOODS EATEN

Time - Note the time at which each item or meal is eaten.

Item - Enter in this column all items (foods, beverages, etc.) consumed, including water. For each item, record any additions made at the time of eating (for example, milk and sugar on cereal, creamer and saccharin added to coffee, seasonings, and butter added to noodles).

Description - If applicable, provide the following for each entry:
- the brand name
- the type or flavor
- the method of cooking
- any other information which may help determine nutrient content

If item is homemade, enter "homemade" and write the recipe at the back of this form (see example).

UNIT OF MEASURE AND AMOUNT

Record only the amount of each item actually consumed.

Describe the foods in terms of tablespoons, teaspoons, cups, ounces, or slices (as bread).

If possible, weigh portions of meat, fish, and poultry.

Record the number of items such as biscuits, English muffins, apples.

State size of canned or bottled liquids. Record drinks in cups or ounces (1 cup = 8 ounces)

Record amount of margarine or butter in teaspoons or tablespoons, (for example, 1 tablespoon on 2 slices of toast). If butter or margarine is used to season vegetables during cooking, record that it was added and the amount (for example, 1 tablespoon added to a 10 ounce package of frozen spinach).

Record the fraction of the whole of a pie, pizza, quiche, cake, etc. (for example, 1/8 pie).

Keep an accurate record of foods consumed away from home.

The information on what you actually consumed will be only as accurate as the information you provide. Accurate and thorough records are needed.

Day of Week Monday

Time	Item of Food or Drink		Description of Item	Unit of Measure	Amount
	Enter all foods and beverages eaten; include any additions made to item at time of eating.		Please include: 1. the make 2. the type or flavour 3. the method of cooking	Enter: dessertspoon, tablespoon, cup, number, etc.	Record number of units eaten.
4:00pm	Menu Item	apple	fresh, red delicious, 3" diameter	each	1
	Addition				
	Addition				
6:00pm	Menu Item	steak	Ribeye, broiled	ounces	3
	Addition	pepper	Food Club	teaspoon	1/4
	Addition				
	Menu Item	rice	Minute, cooked without salt	cups	3/4
	Addition	margarine	Fleischmann's	teaspoons	1
	Addition	parsley	Food Club	teaspoons	1/2
	Menu Item	green beans	cooked from frozen	cups	1/2
	Addition	margarine	Fleischmann's	teaspoons	1
	Addition				
	Menu Item	Tossed Salad			
	Addition	lettuce	Iceberg, shreaded	cups	1
	Addition	tomato	wedges, fresh	3" each	1/4
	Menu Item	cucumbers	fresh	6" each	1/4
	Addition	dressing, fren	Kraft Free	tablespoons	3
	Addition				
	Menu Item	Snickerdoodles	Home made (recipe on back)	each	2
	Addition				
	Addition				
	Menu Item	tea	Peppermint, Celestial Seasonings	8oz cup	1
	Addition	honey	Sure-Bee	teaspoon	1
	Addition				
9:00pm	Menu Item	Water	tap	8oz. cup	1
	Addition				
	Addition				
	Menu Item				
	Addition				
	Addition				

Day of Week ____________________

Time	Item of Food or Drink		Description of Item	Unit of Measure	Amount
	Enter all foods and beverages eaten; include any additions made to item at time of eating.		Please include: 1. the make 2. the type or flavour 3. the method of cooking	Enter: dessertspoon, tablespoon, cup, number, etc.	Record number of units eaten.
	Menu Item				
	Addition				
	Addition				
	Menu Item				
	Addition				
	Addition				
	Menu Item				
	Addition				
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	Menu Item				
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	Addition				

Appendix 8

Form F = Medication Record

Sparrow-MSU Dialysis Study-1990

MEDICATION RECORD

Subject Number: _____ Birthdate: _____ Sex: M F

Please record medications taken by type, day, and time taken. Include any vitamin or mineral supplements you may be taking at this time.

Day	Medication	Time of Day	Taken with

Appendix 9

Form G = Cookie Consumption Record

Sparrow-MSU Dialysis Study-1990

COOKIE CONSUMPTION RECORD - Period II and Period IV

Subject is to complete the form each day of the cookie periods. Mark the appropriate number in the space according to day of week.

Subject Number: _____ Birthdate: _____ Sex: M F

Use the following key to provide information on how and when you ate cookies this week. When did you eat a cookie today?

0 No cookies eaten
1 With a meal
2 Between meals
3 Both ways

What did you consume (if anything) with the cookie?

0 Nothing
A Water
B Soft Drink
C Fruit Juice
D Coffee, Tea, or Hot Beverage
E Other - what?

For example, if you ate Cookie 1 on Day 1 with a meal and coffee you would answer 1 and D.

Day 1	When did you eat it?	What did you consume with the cookie?
Cookie 1	_____	_____
Cookie 2	_____	_____
Cookie 3	_____	_____
Cookie 4	_____	_____

Day 2	When did you eat it?	What did you consume with the cookie?
Cookie 1	_____	_____
Cookie 2	_____	_____
Cookie 3	_____	_____
Cookie 4	_____	_____

Day	When did you eat it?	What did you consume with the cookie?
Cookie 1	_____	_____
Cookie 2	_____	_____
Cookie 3	_____	_____
Cookie 4	_____	_____

Day 4	When did you eat it?	What did you consume with the cookie?
Cookie 1	_____	_____
Cookie 2	_____	_____
Cookie 3	_____	_____
Cookie 4	_____	_____

Day 5	When did you eat it?	What did you consume with the cookie?
Cookie 1	_____	_____
Cookie 2	_____	_____
Cookie 3	_____	_____
Cookie 4	_____	_____

Day 6	When did you eat it?	What did you consume with the cookie?
Cookie 1	_____	_____
Cookie 2	_____	_____
Cookie 3	_____	_____
Cookie 4	_____	_____

Day 7	When did you eat it?	What did you consume with the cookie?
Cookie 1	_____	_____
Cookie 2	_____	_____
Cookie 3	_____	_____
Cookie 4	_____	_____

Appendix 10

Form H = Medical Information Form

Medical Information Form

NAME_____ SUBJECT NUMBER_____
HEIGHT _____

DATE	RUN TIME	WT. ON	WT. OFF	INTERDIALYTIC WT. GAIN	TRANS?	SALINE?

Medical Information Form

NAME:

ADDRESS:
CITY, STATE, ZIP CODE:

PHONE:

SOCIAL SECURITY NUMBER:

DATE OF BIRTH:

SEX:

DIAGNOSIS:

HEIGHT:

WEIGHT:

DIET:

FLUID RESTRICTION:

DATE OF FIRST DIALYSIS:

MEDICATION LIST:

Appendix 11

FORM I = Evaluation of Fiber Research Study

Sparrow Hospital-MSU Dialysis Study

Evaluation of Fiber Research Study

Please complete the following questions as they apply to your participation in the research study.

1. What did you like most about participating in the research study?

_____

_____

_____

2. What (apart for delay of payment) did you like least about participating in the study?

_____

_____

_____

3. Would you participate in a study similar to this one again?

_____Yes _____No Why?

_____

_____

4. Has there been any change in your bowel function since the study ended?
_____Yes _____No Comments:

_____

_____

5. Any comments about the study which you would like to voice at this time?

_____

_____

6. Are there any specific questions you have as a dialysis patient that you think need to be answered using research studies?

_____

Appendix 12

Example of Weekly Checklist

Sparrow Hospital-MSU Dialysis Study

_____ Subject Number

_____ Birthdate

_____ Subject Name

Week 8 - To Do List - Group B

This week: (orange form)

_____ Complete Food and Beverage Record - 1 week day, not on dialysis

_____ Complete Food and Beverage Record - 1 dialysis day

_____ Complete Food and Beverage Record - 1 weekend day (nondialysis)

Day 1 _____

_____ Complete Medication Form (green form)

_____ Complete Daily Record of General Condition (white form)

_____ Eat 4 cookies

_____ Complete Cookie Consumption Record (yellow form)

Day 2 _____

_____ Complete Medication Form (green form)

_____ Complete Daily Record of General Condition (white form)

_____ Eat 4 cookies

_____ Complete Cookie Consumption Record (yellow form)

Day 3 _____

_____ Complete Medication Form (green form)

_____ Complete Daily Record of General Condition (white form)

_____ Eat 4 cookies

_____ Complete Cookie Consumption Record (yellow form)

Day 4 _____

_____ Complete Medication Form (green form)

_____ Complete Daily Record of General Condition (white form)

_____ Eat 4 cookies

_____ Complete Cookie Consumption Record (yellow form)

Day 5 _____

_____ Complete Medication Form (green form)

_____ Complete Daily Record of General Condition (white form)

_____ Eat 4 cookies

_____ Complete Cookie Consumption Record (yellow form)

Day 6 _____

_____ Complete Medication Form (green form)

_____ Complete Daily Record of General Condition (white form)

_____ Eat 4 cookies

_____ Complete Cookie Consumption Record (yellow form)

Day 7 _____

_____ Complete Medication Form (green form)

_____ Complete Daily Record of General Condition (white form)

_____ Eat 4 cookies

_____ Complete Cookie Consumption Record (yellow form)

_____ Complete Cookie Evaluation Record (blue form)

_____ Complete Cookie Acceptance Record (yellow form)

_____ Fast - no food 12 hours before blood sample on Day 8.

Day 8 _____ (Also Day 1 of Week 9)

_____ Fasting Blood Sample will be drawn.

_____ Complete Study Evaluation Form.

List any questions you may have below:

Did you notice any changes in how your medications affected you this week? If so, what?

Completed forms received by:

(name of researcher)

Date

Appendix 13

Recipes

a. Fiber supplement cookies (page 0069 laboratory research manual). (Fiber content per cookie = 3.63 grams, calorie content = 126 calories per cookie) Recipe developed by researchers at Michigan State University including Marci Askegard R. D., and is a modification of a plain sugar cookie recipe developed by A. Worwick, Bronson Methodist Hospital.

Ingredients

1 1/4 cups (140 g) Gold Medal All Purpose Flour
1 cup (240 g) Parkay margarine (stick variety)
1 1/2 cups (300 g) white sugar (common lot)
3/4 cup (180 g) egg substitute (brand name: eggbeaters)
1 teaspoon (3 g) Arm & Hammer baking soda
1/2 teaspoon (1.62 g) French's brand cream of tartar
2 teaspoons (10 ml) vanilla extract
1 2/3 cups (135 g) Fibrad powder
1 tablespoon (15 ml) distilled water

Method of preparation:

1. Preheat oven to 325 F. Grease cookie sheets
2. Weigh dry ingredients using top loading balance. Measure liquid ingredients using graduated cylinders.
3. Sift together dry ingredients, set aside.
4. Beat margarine and sugar with electric mixer until fluffy (2 minutes,25 seconds). Blend in eggbeaters, vanilla, and water with electric mixer (1 minute).
5. Gradually add flour mixture to liquid mixture in two parts blending for 1 minute after each addition of dry ingredients. Mix on lowest seting (fold) for an additional minute.
6. Weigh cookie dough on top loading balance (33.83 g) and drop dough from a spoon. Place 2 inches apart on prepared cookie sheet.
7. Bake at 325 F (for 14 minutes), or until golden brown around edges.
8. Recipe makes approximately 30 cookies.

b. Plain Sugar Cookies (page 0067 laboratory research manual) (fiber content per cookie = 0.24 grams, calorie content = 127 calories per cookie)

Ingredients

2 1/2 cups (280 g)Gold Medal All Purpose Flour
1 cup (240 g) Parkay margarine (softened sticks = 2)
1 1/4 cups (250 g) white sugar (common lot)
3/4 cup (180 g) egg substitute (brand name: eggbeaters)
1 teaspoon (3 g) Arm & Hammer baking soda
1/2 teaspoon (1.62 g) French's cream of tartar
1 1/2 teaspoons (7.5 ml) vanilla extract

Methods of preparation:

Same method of preparation as for the fiber supplement cookies as listed under part a. Methods of Preparation for that cookie for steps 1-5.

6. Weigh cookie dough on top loading balance (30 g), and drop from spoon onto cookie sheet. Place cookies 2 inches apart.
7. Bake at 325 for approximately 13 minutes or until edges are golden brown.
8. Recipe makes approximately 32 cookies.

Appendix 14

Sample of Chem-20, CBC, and Lipoprotein Reports

LIFECHEM Laboratory

PATIENT REPORT

PAGE 1
DATE 10/31/90

ACCOUNT

PHYSICIAN

PATIENT

AGE SEX PRE/POST 373560708 COLLECTED RECEIVED 23630596

TEST NAME	COND. CODE	ABN FLAG	RESULT	UNITS	REFERENCE RANGE	LAB
CBC						ML
WBC		*LO*	4.30	1000/mcL	4.80-10.80	
RBC		*LO*	2.65	mill/mcL	4.70-6.10	
HGB		*LO*	8.9	g/dL	14.0-18.0	
HCT		*LO*	26.7	%	42.0-52.0	
MCV		*HI*	101	mcm3	80-94	
MCH		*HI*	33.7	pg/cell	27.0-31.0	
MCHC			33.5	g/dL	33.0-37.0	
CHEM 20						ML
BUN		*HI*	48	mg/dL	6-19	
CREATININE		*HI*	12.3	mg/dL	0.8-1.6	
POTASSIUM			5.2	mEq/L	3.5-5.3	
SODIUM			135	mEq/L	135-148	
CHLORIDE			104	mEq/L	100-112	
BICARBONATE		*LO*	18	mEq/L	23-29	
CALCIUM			8.9	mg/dL	8.4-10.2	
PHOSPHORUS		*HI*	7.1	mg/dL	2.7-4.5	
ALKALINE PHOS		*HI*	581	U/L	39-117	
GLUCOSE			80	mg/dL	70-105	
AST/GOT			11	U/L	0-37	
ALT/GPT			9	U/L	0-40	
LDH			157	U/L	118-273	
TOTAL BILIRUBIN			0.5	mg/dL	0.1-1.2	
TOTAL PROTEIN			6.7	g/dL	6.5-8.0	
ALBUMIN			4.2	g/dL	3.8-5.2	
URIC ACID		*HI*	7.3	mg/dL	3.4-7.0	
CHOLESTEROL			123	mg/dL	<200	
TRIGLYCERIDE			98	mg/dL	<150	
IRON		*HI*	178	mcg/dL	59-158	
A/G RATIO			1.7		1.0-2.4	
BUN/CREAT RATIO			3.9			
FERRITIN			192	ng/mL	7-350	ML
HDL			34	mg/dL		ML

Suggestive of increased susceptability to Coronary Artery Disease. Male <35 mg/dL & Female <45 mg/dL suggestive of increased susceptibility to Coronary Artery Disease.

Male 35-55 mg/dL & Female 45-65 mg/dL clinical significance not established. Male >55 mg/dL & Female >65 suggestive of decreased susceptibility to Coronary Artery Disease.

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